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Introduction

Detailed knowledge of the chemical processes in plants and animals and in our environment has only been made possible 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 lie in the attomole region and counting individual molecules per unit time has already become a reality. We are making measurements at the level of background contamination. Most samples subjected to chemical analysis are now mixtures, as are even blank samples. With the demand for decreasing detection limits, 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 2,3,7,8-TCDD.

Year	Instrumental technique	Limit of detection [pg]
1967	GC/FID (packed column)	500
1973	GC/MS (quadrupole, packed column)	300
1976	GC/MS-SIM (magnetic instrument, capillary column)	200
1977	GC/MS (magnetic sector instrument)	5
1983	GC/HRMS (double focusing magnetic sector instrument)	0.15
1984	GC/MSD-SIM (quadrupole benchtop instrument)	2
1986	GC/HRMS (double focusing magnetic sector instrument)	0.025
1989	GC/HRMS (double focusing magnetic sector instrument)	0.010
1992	GC/HRMS (double focusing magnetic sector instrument)	0.005
2006	GCxGC/HRMS (using comprehensive GC)	0.0003

Capillary gas chromatography is today the most important analytical method in organic chemical analysis for the determination of individual substances in complex mixtures. Mass spectrometry 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 processes and finally for confirmation of the facts. The complete integration of mass spectrometry and gas chromatography

into a single GC/MS system has shown itself to be synergistic in every respect. While at the beginning of the 1980s mass spectrometry 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 mass spectrometry became more widely recognised and furthermore an indispensable detection procedure for gas chromatography. 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 have made GC/MS important for a broad spectrum of applications. Benchtop GC/MS systems have completely replaced in many applications the stand-alone GC with selective detectors today. Out of a promising process for the expensive explanation of spectacular individual cases, a universally used analytical routine method has developed within a few years. The serious reservations of experienced spectroscopists wanting to keep mass spectrometry within the spectroscopic domain, have been found to be without substance because of the broad success of the coupling procedure. The control of the chromatographic procedure 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. At this point the circle goes back to the earlier reservations of renowned spectroscopists.

The high performance of gas chromatography lies in separation of the substance mixtures. With the introduction of fused silica columns GC has become the most important and powerful method of analysing complex mixtures of products. GC/MS accommodates the current trend towards multimethods or multicomponent analyses (e. g. of pesticides, solvents etc) in an ideal way. Even isomeric compounds, which are present, for example in terpene mixtures, in PCBs and in 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 turn-round time and thus guarantees a high productivity with a high sample throughput. Adaptation and optimisation 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 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 gas chromatography. 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. 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. It is incomprehensible that, in spite of an obvious detection problem, HPLC is still frequently used in parallel to GC/MS to determine polyaromatic hydrocarbons in the same sample.

The coupling of gas chromatography with mass spectrometry 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 pesticides 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 realisation 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. The optimised carrier gas streams show good compatibility with mass spectrometers. Coupling can therefore take place easily by directly connecting the GC column to the ion source of the mass spectrometer. The operation of the GC/MS instrument can be realised because of the low carrier gas flow in the widely used benchtop instruments even with a low pumping capacity. Only small instruments are therefore necessary, and these also accommodate a low pumping capacity. A general knowledge of the construction and stable operating conditions forms the basis of smooth and easily learned service and maintenance. Compared with GC/MS coupling, LC/MS coupling, for example, is still much more difficult to control, not to mention the possible ion suppression by matrix effects.

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. 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. Even today the headspace and purge and trap techniques, thermodesorption, SPME (solid phase microextraction) or SFE (supercritical fluid extraction) are coupled on-line with GC/MS and got further miniaturized and integrated stepwise into the data system for smooth control. Development will continue in this area in future, and as a result will move the focus from the previously expensive mass spectrometer to the highest possible sample throughput and will convert positive substance detection in the mass spectrometer into an automatically performed evaluation.

The high information content of GC/MS analyses requires powerful computers with intelligent programs to evaluate them. The evaluation of GC/MS analyses based on data systems is therefore a necessary integral component of modern GC/MS systems. Only when the evaluation of mass spectrometric and chromatographic data can be processed together can the performance of the coupling process be exploited to a maximum by the data systems. In spite of the state of the art computer systems, the performance level of many GC/MS data systems has remained at the state it was 20 years ago and only offers the user a coloured data print-out. The possibilities for information processing have remained neglected on the part of the manufacturers and often still require the use of external programs (e.g. the characterisation of specimen samples, analysis of mixtures, suppressing noise etc).

Nonetheless development of software systems has had a considerable effect on the expansion of GC/MS systems. The manual evaluation of GC/MS analyses has become practically

impossible because of the enormous quantity of data. A 60-minute analysis with two spectra per second over a mass range of 500 mass units gives 3.65 million pairs of numbers! The use of good value but powerful PCs allows the systems to be controlled but gives rapid processing of the relevant data and thus makes the use of GC/MS systems economically viable.

The Historical Development of the GC/MS Technique

The GC/MS technique is a recent process. The foundation work in both GC and MS which led to the current realisation was only published between the middle and 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 the required level for the once specialised process 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 ionisation 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-focusing mass spectrometer with electrostat and magnetic sector.
- 1934 Mattauch and Herzog published the calculations for an ion optics system with perfect focusing 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 ionisation 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 ICR instruments.
- 1950 Gohlke published for the first time the coupling of a gas chromatograph (packed column) with a mass spectrometer (Bendix TOF, time of flight).
- 1950 The Nobel Prize for chemistry was awarded to Martin and Synge for their work on gas liquid chromatography (1941).
- 1950 From 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 coworkers presented an experimental gas chromatograph to theACHEMA in Frankfurt; parallel work was carried out by Janák in Czechoslovakia.
- 1952 Martin and James published the first applications of gas liquid chromatography.
- 1953 Johnson and Nier published an ion optic with a 90° electric and 60° magnetic sector, which, because of the outstanding focusing 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 time of flight (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 information 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 gas chromatography.
- 1958 Lovelock developed the argon ionisation 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 analysers (Quad 200 RGA) by Bob Finnigan and P.M. Uthe at EAI (Electronic Associates Inc., Paolo Alto, California).
- 1966 Munson and Field published the principle of chemical ionisation.
- 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 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.
- 2000 A. Makarov published a completely new mass analyzer 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 and very high resolution and accurate mass measurement on the chromatographic time scale.