Hans-Joachim Hübschmann

Handbook of GC/MS

Fundamentals and Applications

Second, Completely Revised and Updated Edition

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Hans-Joachim Hübschmann
Handbook of GC/MS

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Second, Completely Revised and Updated Edition

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Dedicated to my wife Gudrun
and my children Maren, Colja, Jessica and Sebastian

Foreword

It is an excellent move that you look into this book!

Analytical chemists want to be efficient and rapid: we are interested in a given task and the results should be available the next morning. This suggests taking the simplest route: "inject and see", there is no time to fiddle about technology! The vendor of the possibly expensive instrumentation might have highlighted the simplicity of his apparatus.

This is a fundamental error. Efficient analysis presupposes a significant amount of time being devoted to understanding the method and the instrumentation. Not doing this in the beginning all too often exacts a high price at a later stage, e.g. in terms of a laborious and awkward method, endless troubleshooting and poor results.

Knowledge of the technology is a prerequisite to make the best choices for a straight and simple method – from sample preparation to injection, chromatographic resolution and detection. If we are honest, we know that a staggering amount of our time is lost to troubleshooting, and unless we have a deep insight into the technology, this troubleshooting is likely to be frustrating and ineffective (problems tend to recur). Hence investing time into understanding the technology is a wise investment for rapid (and reliable) analysis.

Additionally, efficient analysts devote a substantial part of their time to keeping up with technology in order to keep their horizons open: we cannot always anticipate what might be useful tomorrow, and a brilliant alternative may not come to mind if one were not acquainted with the possibility beforehand. To investigate technology only in the context of a given, possibly urgent task is shortsighted. Admittedly, it takes discipline to absorb technical information when the current necessity may not be immediately apparent. However, it pays back many times. It may also be difficult to convince a boss that the investment into reading basic texts and experimenting with puzzling phenomena is essential to be an efficient analyst – unless he was an analyst himself and knows firsthand the demanding nature of analytical chemistry!

It is great that an old hand in the field like Hans-Joachim Hübschmann took his time to bring the present knowledge into such a concise and readable form.

Continue reading!

Fehraltorf, Switzerland *Koni Grob*
May 2008

Preface to the Second Edition

Mass spectrometers identify and quantify molecules by the direct detection of the ionized species. This is in contrast to many other analytical methods that measure the interaction with a molecule e.g., magnetic resonance or UV extinction. The unbiased, highly selective detection of either an accurate mass, or structural fragmentation reactions, makes MS today, more than ever, an indispensable analytical tool to achieve highest accuracy and ultimate compound confirmation. Mass spectrometry in hyphenation with gas or liquid chromatography has become the success story in analytical instrumentation, covering a never expected wealth of applications, from daily routine quality control, to confirmatory analysis with legal impact.

Chromatography, in this context, is often not at the top of the list when discussing GC/MS technologies, but has received increased attention through its role as the technology driver towards new and further extended GC/MS applications. Emerging and newly developed sampling technologies have found increased use in routine applications such as instrumental online cleanup strategies, large volume injection techniques, and the strong bias to increased speed of chromatographic separations. The common endeavour of many new trends is speed of analysis, especially in the quest for a reduced sample cleanup to allow higher throughput at a lower cost of analysis. Clear evidence of the current vitality index in chromatography is the increased participation and high number of contributions at international and local analytical conferences with presentations on well-prepared solutions covering a large diversity of application areas.

Obviously, the pendulum is swinging back from an "everything is possible" LC/MS approach towards GC/MS for proven solutions. This is not for sensitivity reasons but because of the practical approach providing a very general electron ionisation technique compared to the often experienced ion suppression effects known from electrospray LC/MS ion generation. The increased requirement for target compound analysis in trace analysis with legal implications further consolidates the vital role of GC/MS for the analysis of volatile and semi-volatile compounds, as this is the typical situation, e.g., in food safety and doping applications.

Selectivity is key. Sufficient sensitivity for standard and clean samples is a technical minimum requirement and is not the critical issue for employing GC/MS instrumentation any more. Reliable quantitation in complex matrix samples at the lowest limits, and certainly the compliance to international regulations, is driving methodologies forward. Due to the increased requirement for multi-component trace determinations in critical matrices, and the high cost for manual sample preparation, the high target compound selectivity of the mass

spectrometer is increasingly required. In this context, instrumental off-line and even more on-line sample preparation using pressurizes liquid extractions, and online LC-GC pre-separations or solid phase extractions, have become a major trend that is expected to grow further. Highly efficient ionization and selective analyzer technologies, including MS/MS and accurate mass capabilities will advance GC/MS into even higher integrated sample preparation solutions.

GC/MS has expanded rapidly into new areas of application, not leaving development in the known traditional use aside. Environmental analysis has become important as never before, partly due to the implementation of the UN Stockholm Convention Program on persistent organic pollutants. Forensic and toxicological analysis covering drug screening, tracing of drugs and explosives and general unknown analysis, petrochemical applications with the task of crude oil maturity analysis for new exploration sites, and the pharmaceutical applications for quality control, counterfeit and the investigation of natural products, metabolism and kinetics are still challenging applications.

Fairly new challenges arise from the widespread tasks in homeland security to quickly identify chemicals hazardous to human health and the environment, e.g., with the large number of pesticides or toxins as ricin. For food safety assurance GC/MS and LC/MS became the most widely applied analytical techniques for trace and residue analysis. The global trade of food and feed together with the increased public awareness of food safety issues combined with a global brand recognition, generated a primary focus on regulatory compliance testing and law enforcement as a global analytical challenge, not only for GC/MS.

The second English edition of the Handbook of GC/MS accommodates the new trends in GC/MS with a significant revision and extension covering emerging new techniques and referencing recent leading applications. With regard to sample preparation, new pressurized fluid extraction and online solid phase solutions have been added. New separation strategies with fast GC, multidimensional gas chromatography and column switching are covered both in the fundamental section as well as featuring important applications. The section mass spectrometry has been expanded with a focus on increased and high resolution and accurate mass analyser techniques, including time-of-flight and accurate mass quantifications using isotope dilution and lock mass techniques.

The applications section of the Handbook received a major revision. A number of new leading applications with a special focus on widely employed environmental, forensic and food safety examples including isotope ratio mass spectrometry monitoring are discussed. Special focus was put on multi-component analysis methods for pesticides using fast GC and highly selective MS/MS methods. A fast GC application using high resolution GC/MS for the European priority polyaromatic hydrocabons is referenced.

The strengths of automated and on-line SPE-GC/MS method are featured for contaminants from water using multidimensional GC. Other new SPME applications are demonstrated with the determination of polar aromatic amines and PBBs. Another focal point with the presentations of new key applications is the analysis of dioxins, PCBs and brominated flame retardants PBDEs with examples of the congener specific analysis of technical mixtures, the application of fast GC methods and the isotope dilution quantitation for confirmatory analysis.

The identification and quantitation of toxins with the analysis of trichothecenes and other mycotoxins is covering as well such poisoning cases with the highly poisonous toxin ricin, that became of highest public interest due to several recently reported incidents. An exciting

extension of GC/MS to high boiling and polymer substances by analytical pyrolysis is described by the analysis of glycol and derivatives, the characterization of natural waxes and the quantitative pyrolysis polymers.

This expanded and even more comprehensive compilation of up-to-date technical GC/MS fundamentals, operational know-how and shaping practical application work could not have been accomplished without the great support of many specialists and practising experts in this field. Sincere thanks for valuable discussion and provision of data and recent publications for review go to Jan Blomberg (Shell International Chemicals B.V., Amsterdam, The Netherlands), William Christie (The Scottish Crop Research Institute SCRI, Invergowrie, Dundee, Scotland), Inge de Dobeleer (Interscience B.V., Breda, Netherlands), Werner Engewald (Leipzig University, Institute of Analytical Chemistry, Leipzig, Germany), Konrad Grob (Kantonales Labor Zürich, Switzerland), Thomas Läubli (Brechbühler AG, Schlieren, Switzerland), Hans-Ulrich Melchert (Robert Koch Institute, Berlin, Germany), Frank Theobald (Environmental Consulting, Cologne, Germany), Nobuyoshi Yamashita (National Institute of Advanced Industrial Science and Technology AIST, Tsukuba, Japan). For the generous support with the permission to use current application material I also would like to thank Peter Dawes (SGE, Victoria, Australia) and Wolfgang John (Dionex GmbH, Idstein, Germany).

The helpful criticism and valuable contributions of many of my associates at Thermo Fisher Scientific in Austin, Bremen, Milan and San Jose notably Andrea Cadoppi, Daniela Cavagnino, Meredith Conoley, Dipankar Ghosh, Brody Guggenberger, Joachim Gummersbach, Andreas Hilkert, Dieter Juchelka, Dirk Krumwiede, Fausto Munari, Scott T. Quarmby, Reinhold Pesch, Harry Richie, Trisa C. Robarge and Giacinto Zilioli is gratefully acknowledged. Their experience in well-versed applications and critical technical discussions always provided a stimulating impact on this project.

It is my pleasure to thank the many colleagues and careful readers of the first issues whose kind comments and encouragement have aided me greatly in compiling this new revised 2nd edition of the Handbook of GC/MS.

Sprockhövel, July 2008 *Hans-Joachim Hübschmann*

Despite all efforts, errors or misleading formulations may still exist. The author appreciates comments and reports on inaccuracies to allow corrections in future editions to the correspondence email address: Hans-Joachim.Huebschmann@Thermofisher.com

Preface to the First Edition

More than three years have elapsed since the original German publication of the Handbook of GC/MS. GC/MS instrument performance has significantly improved in these recent years. GC/MS methodology has found its sound place in many "classical" areas of application of which many application notes are reported as examples in this handbook. Today the use of mostly automated GC/MS instrumentation is standard. Furthermore GC/MS as a mature analytical technology with a broad range of robust instruments increasingly enters additional analytical areas and displaces the "classical" instrumentation.

The very positive reception of the original German print and the wide distribution of the handbook into different fields of application has shown that comprehensive information about functional basics as well as the discussion about the practical use for different applications is important for many users for efficient method development and optimization.

Without the support from interested users and the GC/MS community concerned, the advancement and actualisation of this handbook would not be possible. My special thanks go to the active readers for their contribution to valuable discussions and details. Many of the applications notes have been updated or replaced by the latest methodology.

I would like to express my personal thanks to Dr. Brody Guggenberger (ThermoQuest Corp., Austin, Texas), Joachim Gummersbach (ThermoQuest GmbH, Egelsbach), Gert-Peter Jahnke (ThermoQuest APG GmbH, Bremen), Prof. Dr. Ulrich Melchert (Robert-Koch-Institut, Berlin), Dr. Jens P. Weller (Institut für Rechtsmedizin der Medizinischen Hochschule, Direktor Prof. Dr. med. H. D. Tröger, Hannover), and Dr. John Ragsdale jr. (ThermoQuest Corp., Austin, Texas) for their valuable discussions and contributions with application documentation and data.

My sincere thanks to Dr. Elisabeth Grayson for the careful text translation.

I wish all users of this handbook an interesting and informative read. Comments and suggestions concerning further improvement of the handbook are very much appreciated.

Sprockhövel, August 2000 *Hans-Joachim Hübschmann*

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1
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 surpression 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 online 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 the ACHEMA 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.

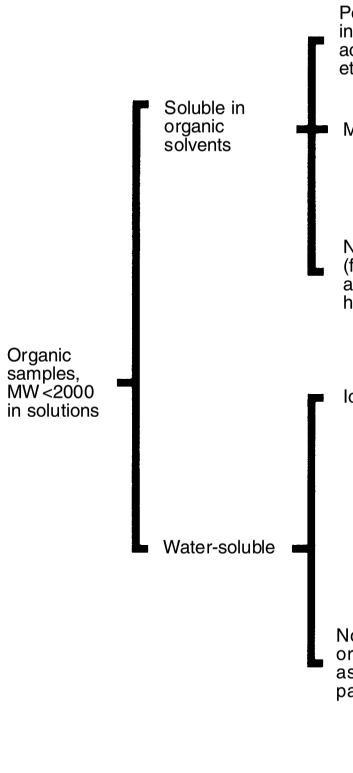
2
Fundamentals

2.1
Sample Preparation

The preparation of analysis samples is today already an integral part of practical GC/MS analysis. The current trend is clearly directed to automated instrumental techniques and limits manual work to the essential. The concentration processes in this development are of particular importance for coupling with capillary GC/MS, as in trace analysis the limited sample capacity of capillary columns must be compensated for. It is therefore necessary both that overloading of the stationary phase by the matrix is avoided and that the limits of mass spectrometric detection are taken into consideration. To optimise separation on a capillary column, strongly interfering components of the matrix must be removed before applying an extract. The primarily universal character of the mass spectrometer poses conditions on the preparation of a sample which are to some extent more demanding than those of an element-specific detector, such as ECD or NPD unless highly selective techniques as MS/MS or high resolution accurate measurements are applied. The clean-up and analyte concentration, which forms part of sample preparation, must therefore in principle always be regarded as a necessary preparative step for GC/MS analysis. The differences in the concentration ranges between various samples, differences between the volatility of the analytes and that of the matrix and the varying chemical nature of the substances are important for the choice of a suitable sample preparation procedure.

Off-line techniques (as opposed to on-line coupling or hyphenated techniques) have the particular advantage that samples can be processed in parallel and the extracts can be subjected to other analytical processes besides GC/MS. On-line techniques have the special advantage of sequential processing of the samples without intermediate manual steps. The on-line clean-up allows an optimal time overlap which gives the sample preparation the same amount of time as the analysis of the preceding sample. This permits maximum use of the instrument and automatic operation.

On-line processes generally offer potential for higher analytical quality through lower contamination from the laboratory environment and, for smaller sample sizes, lower detection limits with lower material losses. Frequently total sample transfer is possible without taking aliquots or diluting. Volatility differences between the sample and the matrix allow, for example, the use of extraction techniques such as the static or dynamic (purge and trap) headspace techniques as typical GC/MS coupling techniques. These are already used as on-line techniques in many laboratories. Where the volatility of the analytes is insufficient, other



	Separating mechanism[1]	Column[2]	Eluent[3] [4]
Polar (soluble in methanol, acetonitrile, ethyl acetate)	NPC	Cyano (CN) Diol (COHCOH) Amino (NH_2) 1°,2°-amino (NH_2NH)	Hexane Chloroform Dichloromethane Acetone Methanol
Moderately polar	LSC	Kieselgur (SiOH) Silica gel (SiOH) Florisil® (SiO_n) Aluminium oxide (Al_2O_3)	Hexane Chloroform Dichloromethane Ethyl acetate
Nonpolar compounds (from aqueous solutions and soluble in hexane, heptane and chloroform)	RPC	Octadecyl (C_{18}) Octyl (C_8) Cyclohexyl (CH) Phenyl (C_6H_5) Cyano (CN)	Hexane Dichloromethane Acetone Acetonitrile Methanol Water
Ionic: Cationic / Anionic	IEC	Cyano (CN) Carboxylic acid (COOH) Benzenesulfonic acid ($C_6H_5SO_3H$) Amino (NH_2) 1°,2°-amino (NH_2NH) Quaternary ammonium (N^+)	Acids Bases Buffers
Nonionic or existing as ion pairs: Polar	NPC	Cyano (CN) Diol (COHCOH) Amino (NH_2) 1°,2°-amino (NH_2NH)	Hexane Chloroform Dichloromethane Acetone Methanol
Nonionic or existing as ion pairs: Moderately polar	LSC	Kieselgur (SiOH) Silica gel (SiOH) Florisil® (SiO_n) Aluminium oxide (Al_2O_3)	Hexane Chloroform Dichloromethane Ethyl acetate Methanol
Nonionic or existing as ion pairs: Nonpolar	RPC	Octadecyl (C_{18}) Octyl (C_8) Cyclohexyl (CH) Phenyl (C_6H_5) Cyano (CN)	Hexane Dichloromethane Acetone Acetonitrile Methanol Water

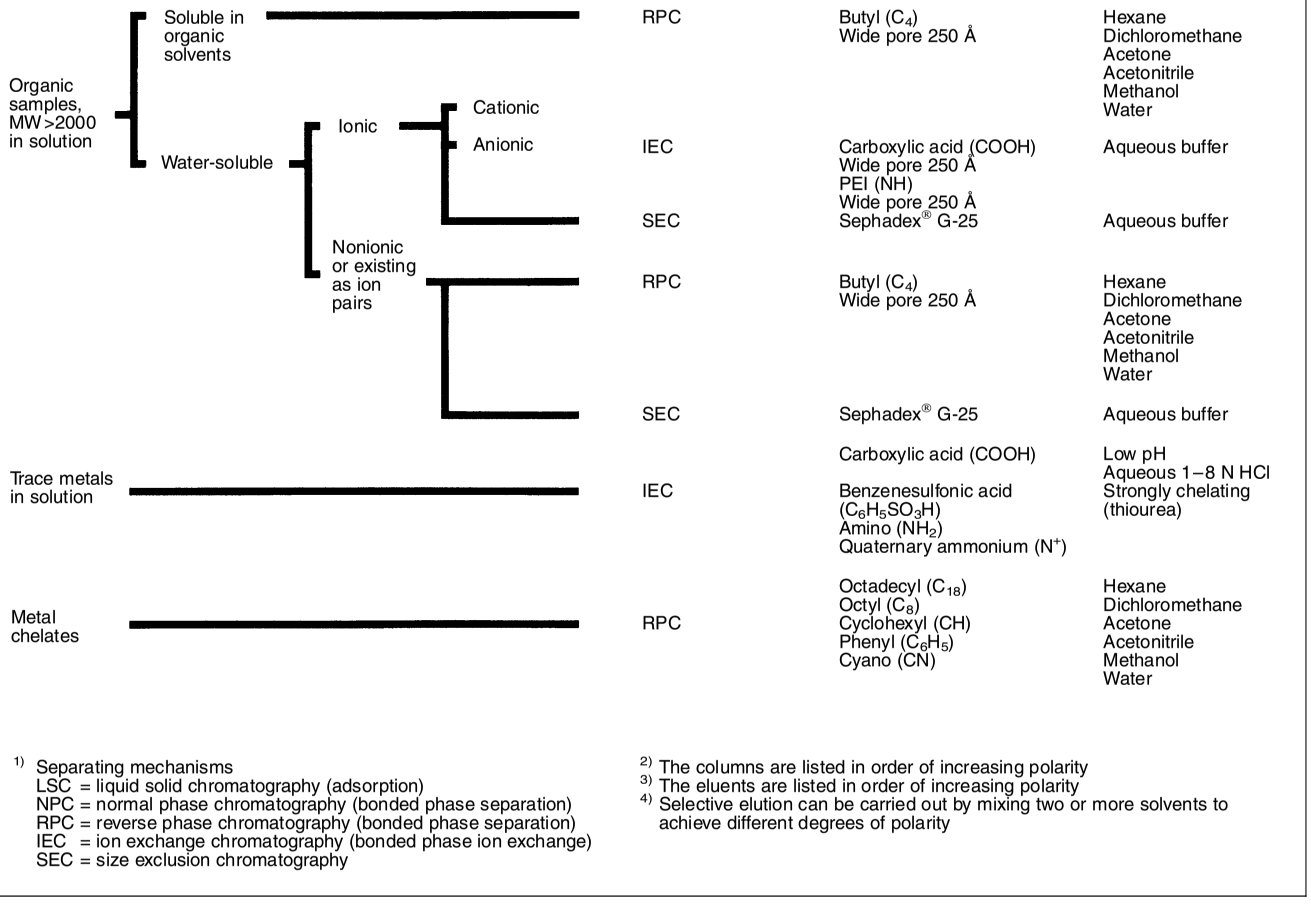


Fig. 2.1 Key to choosing SPE columns and eluents. The choice of the SPE phase depends on the molecular solubility of the sample in a particular medium and on its polarity. The sample matrix is not considered (J. T. Baker).

extraction procedures e.g. thermal extraction, pyrolysis or online SPE techniques are being increasingly used on-line. Solid phase extraction in the form of microextraction, LC/GC coupling, or extraction with supercritical fluids show high analytical potential here.

2.1.1 Solid Phase Extraction

From the middle of the 1980s solid phase extraction (SPE) began to revolutionise the enrichment, extraction and clean-up of analytical samples. Following the motto 'The separating funnel is a museum piece', the time-consuming and arduous liquid/liquid extraction has increasingly been displaced from the analytical laboratory. Today the euphoria of the rapid and simple preparation with disposable columns has lessened as a result of a realistic consideration of their performance levels and limitations. A particular advantage over the classical liquid/liquid partition is the low consumption of expensive and sometimes harmful solvents. The amount of apparatus and space required is low for SPE. Parallel processing of several samples is therefore quite possible. Besides an efficient clean-up, the necessary concentration of the analyte frequently required for GC/MS is achieved by solid phase extraction.

In solid phase extraction strong retention of the analyte is required, which prevents migration through the carrier bed during sample application and washing. Specific interactions between the substances being analysed and the chosen adsorption material are exploited to achieve retention of the analytes and removal of the matrix. An extract which is ready for analysis is obtained by changing the eluents. The extract can then be used directly for GC and GC/MS in most cases. The choice of column materials permits the exploitation of the separating mechanisms of adsorption chromatography, normal-phase and reversed-phase chromatography, and also ion exchange and size exclusion chromatography (Fig. 2.1).

The physical extraction process, which takes place between the liquid phase (the liquid sample containing the dissolved analytes) and the solid phase (the adsorption material) is common to all solid phase extractions. The analytes are usually extracted successfully because the interactions between them and the solid phase are stronger than those with the solvent or the matrix components. After the sample solution has been applied to the solid phase bed, the analytes become enriched on the surface of the SPE material. All other sample components pass unhindered through the bed and can be washed out. The maximum sample volume that can be applied is limited by the breakthrough volume of the analyte. Elution is achieved by changing the solvent. For this there must be a stronger interaction between the elution solvent and the analyte than between the latter and the solid phase. The elution volume should be as small as possible to prevent subsequent solvent evaporation.

In analytical practice two solid phase extraction processes have become established. Cartridges are mostly preferred for liquid samples (Figs. 2.2 and 2.3). If the GC/MS analysis reveals high contents of plasticisers, the plastic material of the packed columns must first be considered and in special cases a change to glass columns must be made. For sample preparation using slurries or turbid water, which rapidly lead to deposits on the packed columns, SPE disks should be used. Their use is similar to that of cartridges. Additional contamination, e.g. by plasticisers, can be ruled out for residue analysis in this case (Fig. 2.4).

A large number of different interactions are exploited for solid phase extraction (Fig. 2.2). Selective extractions can be achieved by a suitable choice of adsorption materials. If the eluate is used for GC/MS the detection characteristics of the mass spectrometer in particular