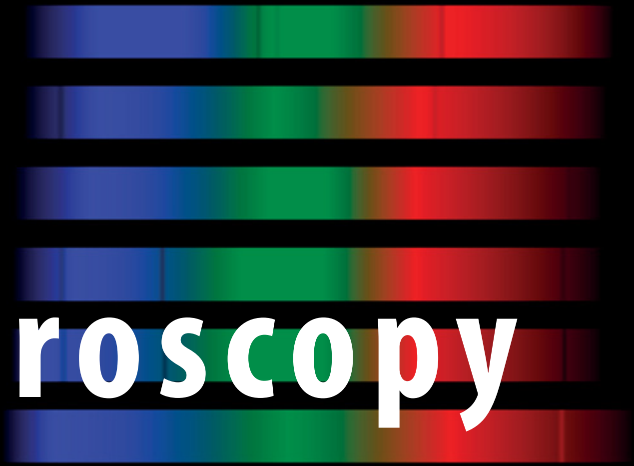
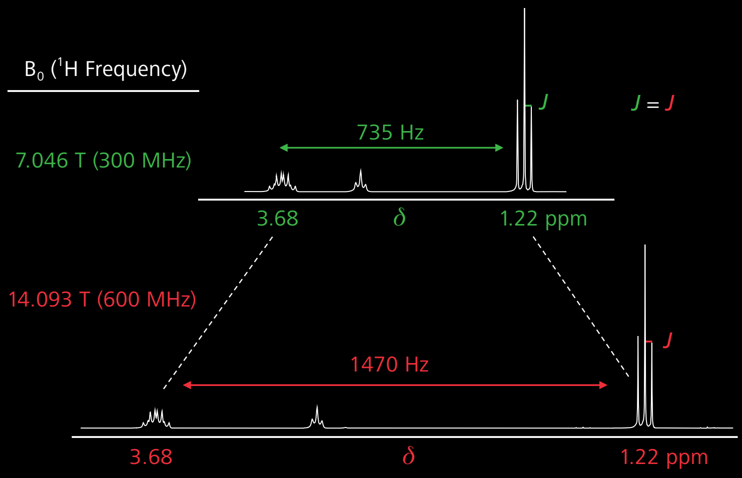
Peter M. Skrabal



Spectroscopy

An interdisciplinary integral description of spectroscopy from UV to NMR




Find the Bruker Way!

Dedicated to my parents, my wife
and my two sons

Peter M. Skrabal

Spectroscopy

An interdisciplinary integral
description of spectroscopy
from UV to NMR

vdf Hochschulverlag AG an der ETH Zürich

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Preface

The author, Dr. Peter Skrabal, places a remarkable and exceptional book into your hands. If spectroscopy has sofar not been closest to your heart, the reading of this book will be particularly profitable and informative. But in case you are a long standing specialist and know already (nearly) all about one of the numerous spectroscopic disciplines, you will discover – perhaps for the first time – surprising correlations between the various spectral regions.

Why has no one before ventured such an integral description of spectroscopy? In reality such an attempt is obvious, since the basic principles of spectroscopy are universal and in all spectral regions the same. For an analytical thinking mind all the spectroscopic experiments are nearly identical. One likes to mention the so-called black box, which by a source of electromagnetic radiation is excited to its natural vibrations. It then only needs a frequency-selective detector to register the spectroscopic answer and one has a functional spectrometer, which delivers illustrative insights into the black box. But as so often the crux of the matter are the various and divergent details!

Peter Skrabal masters the situation in a sovereign way. In the first instance he sets up a bulky unbroken thread through all the spectral regions to emphasize the similarities. And yet he does not flinch from resolving the thread into its so many single fibers, whenever the description of the specific peculiarities of the spectroscopic disciplines require this. And he bundles all these highly individual fibers finally back into a coherent thread. Doubtless there is no better method to understand such a detailed widespread theme in its manifold coherence.

I could imagine that this book could be used very advantageously in teaching undergraduates: at first instance the enormous amount of facts requires the outline of the basic principles. But the book is also very useful for individual studies: it rouses ones interest to formulate relevant questions and to search for explanatory answers.

I hope that this book will bring many new enthusiastic friends into the so powerful and fascinating field of spectroscopy. To the experienced spectroscopist the book offers stimuli to broaden his mind and to discover exciting tours into neighboring disciplines. I wish the readers many unexpected reading pleasures.

Richard R. Ernst
(Nobel Prize in Chemistry 1991)

Zurich, April 22nd, 2009

(translated by the author from the 1st German edition)

Foreword

In consideration of the vast number[1] of books on spectroscopic methods the obvious question emerges: Why another book on spectroscopy?

The intention of this book is a twofold one:

1. It is the result of didactic reflections. Since all the discussed spectroscopic methods root in the reversible absorption of electromagnetic radiation, their common fundamentals are described in a new and, as I believe, in a particularly instructive manner. In contrast to the conventional methodical order a chapter on IR spectroscopy does not follow one on UV/Vis spectroscopy etc. My description of spectroscopies rather follows the unbroken thread of their physical principles, which are common to all these spectroscopic methods. Central chapters therefore are *"The Absorption Processes and their Energies"* and *"The Absorption Intensities: Prerequisites and Consequences"*. This disorder in the conventional methodical sense enables the reader, to directly comprehend the important mutualities and distinctions, such as for example the correlation between the quantities of the absorbed energy amounts and the sensitivities of spectroscopic methods.

The plan for this method of description matured in the course of my experiences during more than 25 years in provision of spectroscopy courses for students of chemical engineering at the Department of Chemistry and Applied Biosciences (D-CHAB)[2] of the Swiss Federal Institute of Technology in Zurich (ETHZ).[3] During these years I have outlined a few hundred transparencies, and a part of these in revised form represents as the Figures the optical guide throughout the book. "My" students have missed this now available textbook. Since time previously did not allow me to write it, I thank them now: they always animated me to improve the transparencies and my comments on them. I hope that some of these motivated students will "stumble" over this book and it will remind them of our many stimulating hours.

2. I have written the book as an introduction for nonspectroscopists. With its new approach it should make students of different disciplines and with different backgrounds (from natural and engineering sciences, of medicine and even of art, human and economic sciences) well acquainted with the basics of spectroscopic methods. For this objective I abandon mathematical and physical derivations as much as appropriate. Nevertheless, the topics of the book require the inquisitiveness of the reader about physical correlations. In this sense the book is particularly qualified to introduce readers with a natural science background into spectroscopy.

In obligation of these objectives it has been a great challenge to encounter the appropriate profundity and precision of descriptions. I am convinced that approaches of this form to all domains of natural sciences are necessary to enable our societies to understand their results. Particularly the results of modern analytical methods are, veiled or very obvious, omnipresent and influence our environment and our daily life: in part positively (e.g. via

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[1] SciFinder Scholar™, American Chemical Society, Washington, DC, USA, Version 2007, found more than 1000 books for the search terms *Spektroskopie* and *spectroscopy* within the period 2001 – 2010.

[2] www.chab.ethz.ch/

[3] www.ethz.ch/

emission controls) and in part negatively (e.g. by the misuse of results from highly sensitive analytical methods in the ppm to ppq range, i.e. parts in 10^6 to 10^{15} parts). Not least the knowledge of these dimensions is the postulate for the correct appraisal of the significance of analytical results.

I thank my former students as well as my colleagues, friends, and teachers:

Dr. Ulrich Sorger from the time of my graduate studies in Graz,

Prof. Richard Kuhn (1900 – 1967), my Ph.D. supervisor at the Max-Planck-Institut für medizinische Forschung (MPImF) in Heidelberg,[1]

Dr. Peter Schütz from the time of my studies at the MPImF in Heidelberg,

Prof. Heinrich Zollinger (1919 – 2005), who offered me the opportunity to research during ca. 20 years at the ETHZ , *i.a.* in the area of chemical reaction mechanisms, and to establish at the same time NMR spectroscopy at the Institute for Chemical and Bioengineering (ICB)[2] at ETHZ,

Dr. Ulrich Meyer and Prof. em. Paul Rys; to them I have been connected in friendship and in research at the ICB over more than 30 years,

Prof. em. Paul S. Pregosin (LAC[3]), with whom I "probed" FT-NMR spectroscopy in the early 1970s,

as well as Dr. Thomas Abend, Dr. Harold Baumann, Prof. em. Hans Dutler, and Prof. em. Helmut Hauser, friends and colleagues at the ETHZ, whom I have been connected with by common research projects and in friendship over many years. With all the aforesaid colleagues, friends, and teachers I have spent innumarable precious hours in scientific and other discussions, which have enriched my life.

Last but not least I thank Prof. em. Richard R. Ernst (ETHZ) for his preface to this book.

Finally, I thank the publisher vdf, in particular Mr. Erich Bärtsch for his help with the editing. And I thank Bruker Biospin AG, Switzerland, for the permission to reproduce some of the Figures.

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Kilchberg ZH, August 2012

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1. www.mpimf-heidelberg.mpg.de/
2. www.icb.ethz.ch/
3. Laboratory of Inorganic Chemistry, ETHZ (www.lac.ethz.ch/)

Content

Content

1 Introduction

1.1 Definitions and Systematics

Spectroscopic methods constitute a central part of modern analytics. The term spectroscopy implies the use of a spectrometer for the registration of spectra. Spectra are the registrations of absorption intensities as functions of specific wavelengths or frequencies of interest within a spectral window of the electromagnetic radiation.

I avoid the term *"*Analytical Chemistry*"*, which is out of date but still in use in various contexts. Its origin dates back to the original classification of chemistry into disciplines like *"*Organic Chemistry*"*, "Inorganic Chemistry*"*, or "Physical Chemistry*"* at the time when analytical methods had been of purely *chemical* nature (such as the acid-base titrations with the help of indicators or the classical elemental analyses by combustion or titration). At those times only physical instruments such as e.g. the balance were available, but no spectrometers. Ernst Abbe (German physicist,1840–1905) provided the scientific basis for the production of the first optical instruments. The distinction between the different chemical disciplines also is outdated, as research in natural sciences over many years has been a matter of *inter*-, *trans*- or *multi*disciplinary approaches. In the sense of *chemical* analytical methods the term *"*Analytical Chemistry*"* of course is still meaningful (see the use in *Fig. 1.1*).

The word spectroscopy derives from the Latin word *spectrum* for picture and the Greek *skopein* for looking at. A comprehensive definition[1] describes spectroscopy as *"the production and investigation of spectra"*, including *"the art or process of using"* a spectrometer, i.e. an instrument, which registers spectra. And spectroscopy is defined as the *"science of spectroscopic phenomena"*. A physical description[2] defines spectroscopy as the *"science that is concerned with the measurement of the emission and absorption spectra of light or other forms of electromagnetic radiation"*.

The terms analytics and analytical derive from the Latin *analyticus* as well as from the Greek *analytikos*, for *"of or relating to the Greek* analysis *..."*. And *analysis* from the Greek *analyein* (to dissolve) means *"separating ... a whole or a compound into its component parts or constituent elements*".[1] George H. Morrison (Cornell University, Ithaca, NY, USA) writes pertinent to the however partly obsolete (see above) entry *Analytical Chemistry*: *"...The scope of analytical chemistry now spans industry, agriculture, the environment, and medicine, as well as many research areas in chemistry, biology, biochemistry, geology, and other physical sciences ....* Analytical chemistry *is the detective of the scientific world ..."*.[2]

Fig. 1.1 illustrates the systematic classification of analytical methods by typical examples. The cited acronyms stand for the following terms. *Separation Techniques*: **G**as-**C**hromatography, **T**hin **L**ayer **C**hromatography, **H**igh **P**erformance **TLC**, **L**iquid **C**hromatography, **H**igh **P**ressure or **P**erformance **LC**, **S**upercritical **F**luid **C**hromatography and **C**apilary **E**lectrophoresis; *Sample Preparation*, *i.a.* for the *Process Control*: **F**low **I**njection **A**nalysis; *Instrumental Methods*, including methods that use a spectrometer or another instrument: **N**uclear **M**agnetic **R**esonance, **E**lectron **S**pin **R**esonance (or **E**lectron **P**aramagnetic **R**esonance EPR), **I**nfra**R**ed, **Vis**ible and **U**ltra**V**iolet, **M**ass **S**pectrometry (or **S**pectroscopy), and for *Surface Analyses*: **A**uger **E**lectron **S**pectroscopy, **E**lectron **S**pectroscopy for **C**hemical **A**nalysis,

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[1] From *Webster's Third New International Dictionary*, G. & C. Merriam Co., Springfield, MA, USA, **1971**, ISBN 978-0-87779-201-7.

[2] From C.G. Morris (Editor), *Academic Press Dictionary of Science and Technology*, Academic Press, San Diego, **1992**, ISBN-10: 0-12-200400-0, ISBN-13: 978-0-12-200400-1.

X-ray **P**hoto **E**lectron (or **E**mission) **S**pectroscopy, **L**ow **E**nergy **E**lectron **D**iffraction. Under the heading *Analytical Chemistry* some *chemical* analytical methods are mentioned: Combustion Analysis, *chemical* Identification of Functional Groups (for example –COOH or –NH_2), and Elemental Analysis, today on the microscale.

One of the pioneers in microanalysis was Fritz Pregl (1869–1930, Austria, 1923 Nobel Prize in Chemistry, “for his invention of the method of micro-analysis of organic substances”). Over the nearly 90 years since that time the demanding manual microanalysis has developed into an instrumental automated analysis.

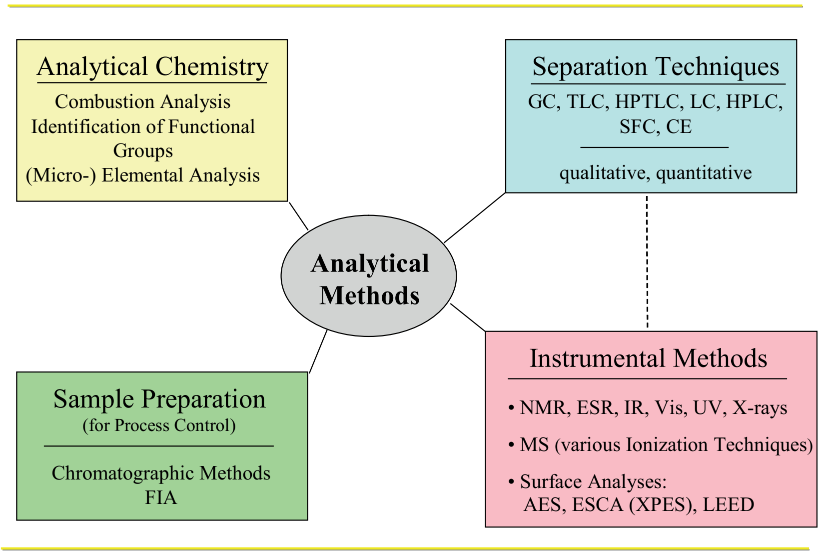

Fig. 1.1. A Systematic Classification of Analytical Methods

The dashed line in *Fig. 1.1* indicates that in most cases as an integral part of the separation techniques an instrument, e.g. an NMR, IR, UV/Vis or mass spectrometer as detector, is utilized. One talks of so-called Tandem- or hyphenated techniques, typically of e.g. LC-NMR or GC-MS. In MS-MS (Tandem-MS) the combination of two mass spectrometers for high resolution is applied. In the Flow Injection Analysis typically UV/Vis or IR spectrometers as detectors are used. In TLC (or HPTLC) quantitative analyses are possible by combination with reflection instead of absorption spectrometers. The sample preparation with the help of chromatographic methods and/or of FIA in this systematic classification is emphasized, since it is of extraordinary importance not only in structure analyses (Chapt. 8.1, p. 208) but also in the industrial analytical process control (Chapt. 1.3, p. 6, and Chapt. 8.2, p. 271ff).

1.2 Structure–Property Relations, Synthesis, and Process Planning

The spectroscopic methods (NMR, ESR, NIR (near IR), IR and UV/Vis spectroscopy) described in this book are in terms of their applications and the interpretations of their results, of unique importance to *every* scientist, who needs information on the structure of molecules or on their concentrations. This applies to small as well as to very large molecules (macromolecules like polymers or biopolymers), and to problems in the gas, liquid, liquid crystalline, or solid phase of the analytes.

In contrast to the question about structures of molecules their concentrations and the interpretations of the latter quasi are an everyday theme that shapes our environment (e.g. aliments, air, water, climate). As a result of the developments of analytical methods during the last decades concentrations of molecules can be measured in the ppt to ppq range (**p**arts **p**er **t**rillion and **q**uadrillion, see *Tab. 3*, p. 320). The spectroscopic methods cover a concentration range of several powers of ten and hence the sample preparation has an essential influence on the sensitivity of measurements (cf. Chapt. 4 and 5.5, p. 95 and 157).

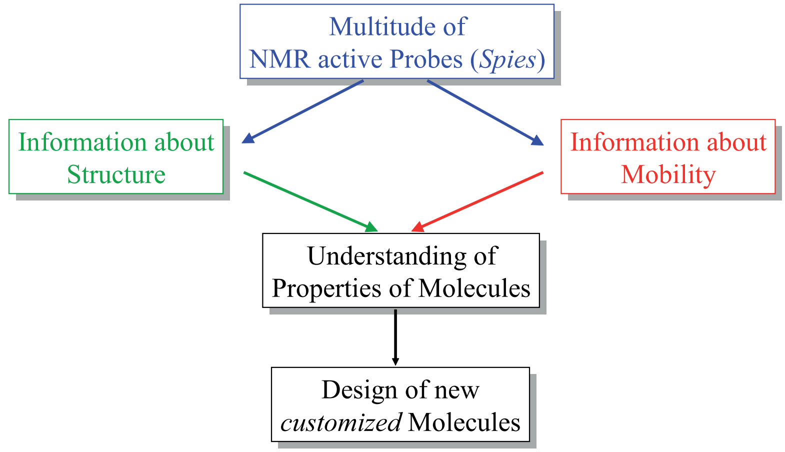

Fig. 1.2.1. QSPR-Information from NMR Spectroscopy

For the layperson the magnitudes of sensitivities hinder the interpretations of results regarding their relevance. Nevertheless, the meaningful utilizations of results stand or fall with these interpretations. Analytical results should comply with the rules of OECD (**O**rganization for **E**conomic **C**o-operation and **D**evelopment)[1] for GLP (**G**ood **L**aboratory **P**ractice). Besides these controlling criteria, which aim at a guarantee of quality and comparability of results, secondly the relevance of measured concentrations must be interpreted in relation to objectives.

The knowledge of structures of molecules (preferably in three dimensions) is a necessary requirement for the first steps on the path to a new product (e.g. a new functional dyestuff, a new polymer, or a new medicament). The first steps on this path require the correlations of structures of molecules with their properties. In *life sciences* such a correlation is known as **Q**uantitative **S**tructure–**A**ctivity **R**elationship (**QSAR**), or **Q**uantitative **S**tructure–**P**roperty **R**elationship (**QSPR**) in general.

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[1] www.oecd.org/home/

Finding the most appropriate path
to a target molecule
with the help of “school knowledge”
relies on chance

1. *Finding* all possible paths
to a target molecule
in a complete **synthesis tree**
with the help of computer programs
(*on the basis of* up to date databases)

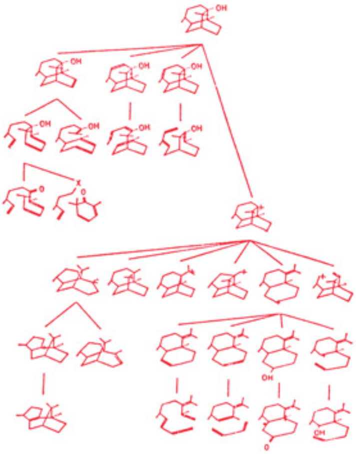


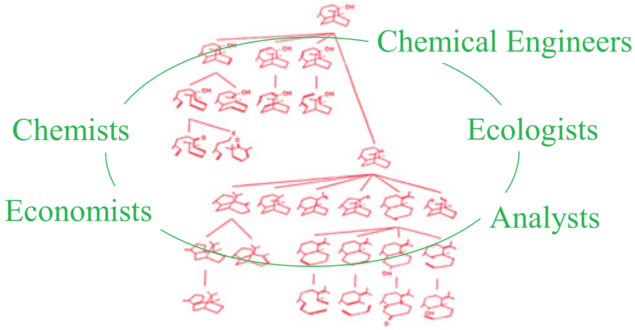
Fig. 1.2.2. Integral Process Development with a Synthesis Tree

Fig. 1.2.1 illustrates the flow of information on structure and mobility of a molecule using the example of nuclear magnetic resonance spectroscopy (NMR) for understanding the molecular properties. The understanding of the properties of structurally similar molecules finally allows the conception of new “customized” molecules. We will learn that NMR spectroscopy is exceptional in that it allows one to investigate the molecule not only in its entirety but also on a “local” atomic scale with the help of the selection of specific “spies” (as IR spectroscopy does, but in contrast to e.g. UV/Vis spectroscopy, cf. Chapt. 8.1, p. 208). These spies are the NMR active atom isotopes like the proton (^{1}H) or the ^{13}C atom. These isotopes are called NMR active probes. Each of the spectroscopic methods contributes its part to the full and total comprehension of the properties of molecules, NMR spectroscopy however (together with ESR spectroscopy for molecules with unpaired electrons – the radicals) offers particularly detailed information.

As a consequence of the immense information derived from analytical methods their impact on the development of industrial products has moved from their analyses *after* the production process (in the first instance the quality control after synthesis) to the *beginning* of the process of planning a new product. QSAR and QSPR partly have led to the point, where nowadays even the target molecule may be defined with the help of analytics.

The course of planning the synthesis of a new product in this modern sense is shown in *Fig. 1.2.2*. It is no longer a course relying on inevitably limited “school knowledge” or the know-how of envolved scientists, but with the help of computer programs and enormous databases one may find the optimal path in a so-called synthesis tree. In this synthesis tree the target molecule is the top and each single structure below in various branches of the tree is a potential intermediate. The roots of the tree constitute the potential starting materials (educts).

2. Evaluation *of the* **synthesis tree**
   (potentially with the help of evaluation programs)



3., 4., ... the usual steps

Fig. 1.2.3. Evaluation of a Synthesis Tree by Various Experts

Figs. 1.2.2 and *1.2.3* show a computer-generated synthesis tree for a natural substance, which dates back to the origin of these developments in the 1960s. In this process a computer program generates all possible paths from a target molecule to each of the individual educts – with arbitrary criteria – by data, which are stored in various immense databases. One talks of this process as retrosynthesis. The data has been collected over decades by countless scientists. The combination and application of this data multitude in a complete synthesis plan with all potential steps requires the help of computer programs which have been developed for this specific purpose. The evaluation of the synthesis tree that follows is *the* challenge for the mentioned experts. However there are evaluation programs in development, which according to predefined criteria search for the best available route of synthesis. The usual steps 3., 4., ... follow – after the selection of the educts – as the necessary steps of synthesis in the laboratory and in pilot plants, in combination with the appropriate analytics.

In this sense in the symbolic depiction in *Fig. 1.2.3* the analyst not only takes part in a discussion with the circle of chemists, chemical engineers, economists and ecologists, who evaluate the synthesis tree to the target molecule, but prior to this discussion, with the analysts help, the *target molecule* has been selected among potential canditates by QSAR or QSPR. One talks of “integral process development”.

Over the past decades the importance of analytical methods in natural and technical sciences with all the consequences for the economy and ecology has led to impressive developments, in regard to financial investments and therefore also in regard to the results. Hence analytics became a very important branch of industry (cf. Chapt. 1.4, p.9).

1.3 Development of Computers, Dynamics of Analytical Methods, and Process Control

Two developments have helped spectroscopic analytics to leverage in all conceivable applications: an enormous increase in sensitivities and a significant shortening of the required times for analysis. Essentially both developments are connected with advances in computer technologies. For instance, the specifications of hard disks as long term and mass storage devices illustrate these advances impressively in *Tab. 1.3*. The reported data should be read as guide values and those for 2006 refer to values for hard disks in notebooks. Besides these advances the ones in processors, main storage (*i.a.* RAM for **R**andom **A**ccess **M**emory), or in bus technologies have been equally important.

Tab. 1.3. Advances in Hard Disk Technology

	1976	**1996**	**2006**
capacity	16 MB	1 GB	> 100 GB
weight	50 kg	0.5 kg	< 0.2 kg
price	50 kFr	0.5 kFr	< 0.1 kFr
access time	30 ms	10 ms	5 ms

Within ca. 30 years the access time (i.e. the reading time) to stored data (as well as the writing time) has been shortened only by the small factor of 1/6. This factor underlies that the reading/writing head must be positioned to the necessary position on hard disks *mechanically*. Therefore, it is conceivable that long term/mass storage hard disks will be complemented and/or substituted by the already available likewise nonvolatile (i.e. independent of power) memory devices on a chip basis (*flash chips* – analogous to the established USB flash drives – on Solid State Disks SSD). Their advantages are mechanical ruggedness, marginal power consumption, and access times of µs. The access times of USB flash drives are limited by the serial interface USB (*Universal Serial Bus*). At present the disadvantages of SSD are mean writing times, a comparatively high price, and their erosion (ca. 10^5 writing processes). New developments integrate these SSDs into the internal bus structure, substituting the conventional hard disks and therefore avoiding slow interfaces like USB (e.g. in the recent *MacBook Air* from Apple). And even faster storage media (with access times in the ns range) are under development (e.g. the so-called *racetrack* devices).

In the last millennium for several decades a pioneer and critical observer of the developments of analytical methods, in view of their scientific as well as industrial importance, was H. Michael Widmer (1933–1997, ETHZ and Ciba-Geigy AG, Basel). His columns in the journal *Chimia*[1] are most likely well known to every analyst in German-speaking countries. He regularly reported on the developments of analytical methods (therefore of course on PITTCON, the ***Pitt****sburgh* ***Con****ference on Analytical Chemistry and Applied Spectroscopy*, one of the most important annual analytics expositions). He had been competent to do so, since he was an analyst, who himself conducted pioneering scientific work with his research group. His contributions to the developments of e.g. the so-called µ-TAS (micro-**T**otal chem-

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[1] www.chimia.ch.

ical **A**nalytical **S**ystems, *i.a.* the combined FIA techniques, *cf.* Chapt. 8.2, p. 271ff) and other analytical chips in the sense of integrated analytical μ-components have been seminal. Following his more than 100 scientific papers in 1998 *quasi* as his legacy, for education in analytics a Curriculum of the FECS (**F**ederation of **E**uropean **C**hemical **S**ocieties) was published.[1] Since I had been acquainted with H. M. Widmer, he enabled annual excursions for "my" students into his research group at Ciba-Geigy AG in Basel. These insights into industrial analytical research had been most impressive and continued over many years.

Figs. 1.3.1 and *1.3.2* illustrate the developments far into the 1980s and provide an example of spectroscopic reaction monitoring. In the first place a crucial factor for the success of analytical methods in *industrial* applications was their increase in speed. As *Fig. 1.3.1* – using the examples of GC and LC – demonstrates, both separation methods fell below the former threshold value of innovation of ca. 60 s only in the 1980s. The step below this value allowed the transition from retrospective (i.e. analysis of the product *after* the end of the production process) to diagnostic analysis (*during* the production process) on the time scale of seconds, *i.a.* with the help of the combination of FIA and **TOF**-MS (**T**ime **O**f **F**light MS, i.e. discrimination of ions with different mass/charge ratios m/z via their flight time from the ion source to the detector).

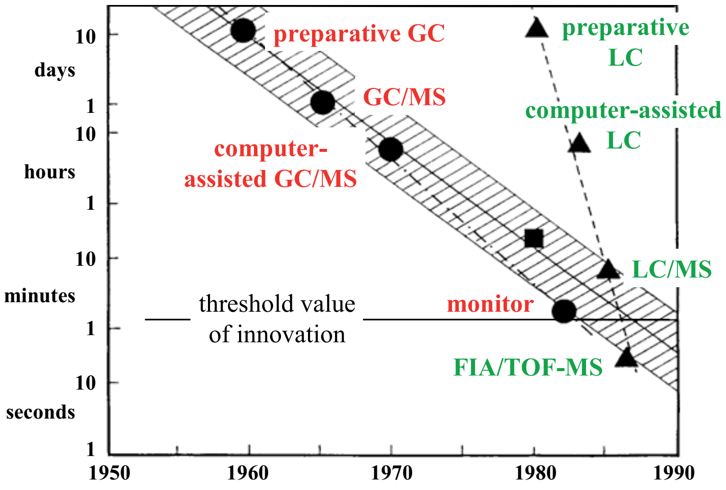

Fig. 1.3.1. Development of Analytical Methods in Relation to Time Requirement

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[1] R. Kellner, J.-M. Mermet, M. Otto, H.M. Widmer (Eds.), *Analytical Chemistry*: *The Approved Text to the FECS Curriculum Analytical Chemistry*, Wiley-VCH, Weinheim, **1998**; 2nd Ed.: J.-M. Mermet, M. Otto, M. Valcárcel (Eds.), *Analytical Chemistry, A Modern Approach to Analytical Science*, R. Kellner, H.M. Widmer (founding Eds.), Wiley-VCH, Weinheim, **2004**, ISBN 3-527-30590-4.

Classical GC and LC (even with computer-assisted evaluations of results), preparative (meaning the separation of amounts in the mg to kg range, which allows for continuous processing of the separated components) or analytical, had been limited to manual sampling. Today the so-called monitors with automated feeding of a partial gas flow to the detector in GC or the automatic sampling by means of FIA (e.g. with the necessary dilution of samples) in LC allow the analysis and evaluation of the analytical results within seconds.

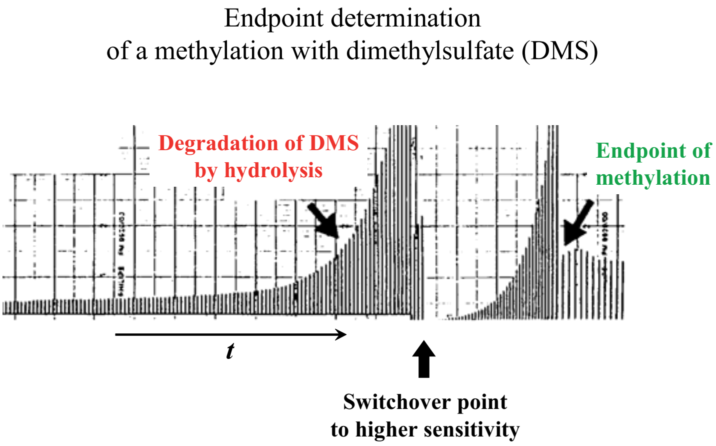

Fig. 1.3.2. On-line *Detected Endpoint of a Methylation Reaction*

Therefore nowadays the chemical industry is able to operate within borders that are determined by the instrumental analytical methods. This allows process control in the interest of product quality, safety, industrial hygiene, and emission controls. The so-called MAC values (**M**aximum **A**llowable **C**oncentrations) can be measured no longer only in ppm (10^{-6} g/g), but in ppq (10^{-15}g/g). The final quality control of the end product ideally is complemented by monitoring analytes of processes in flowing material systems (e.g. FIA via optical fibers combined with UV/Vis or IR spectrometers). In this sense the common terms *on-line*, *in-line*, and *in-time* for the type of analytical process controls have to be understood. H. M. Widmer had used the term "soft chemistry" (*sanfte Chemie*), which refers to these process controls with all the immense benefits for safety, industrial hygiene, reduced amounts of waste products, and for emission control. Modern analytics are an impressive example of fundamental research that is not primarily "profit-oriented". Although at the beginning successful application areas for results can be sensed on the distant horizon, they cannot be *planned*.

Particularly impressive in regard to this statement stands NMR spectroscopy with its at the beginning not foreseeable potential in all areas of research, technology, and medical science. Four Nobel Prizes have been awarded: to F. Bloch[1] together with E. M. Purcell[2] (1952), R. R. Ernst[3] (1991), K. Wüthrich[4] (2002, together with J. B. Fenn and K. Tanaka) and to P. C. Lauterbur[5] together with Sir P. Mansfield[6] (2003). The pioneers of the experimental confirmation of the NMR phenomenon, Bloch and Purcell, most likely had not even dreamed of its application in the MRI technique (**M**agnetic **R**esonance **I**maging). Nuclear magnetic resonannce imaging today constitutes an invaluable part of diagnostic medicine (recognizing deseases), not only in regard to imaging but also in the qualitative and quantitative analysis of metabolic processes.

Fig. 1.3.2 of a methylation reaction (i.e. the introduction of a methyl group $-CH_3$) with the help of dimethylsulfate (DMS, $CH_3OSO_2OCH_3$), the methylester of sulfuric acid (H_2SO_4 or $HOSO_2OH$), shows the continuously *in-time* and *on-line* monitored endpoint. Details of such results naturally are and will not be published in the interests of patent protection. However, for the qualitative understanding of the diagram thus much: at the end of the methylation reaction there is excessive DMS. The excess of DMS indicates the endpoint of the methylation and one of the hydrolysis products of DMS, e.g. sulfuric acid, is monitored (e.g. by optical spectroscopy and with the help of a pH-indicator).

1.4 Economic Significance of Analytical Methods

The increase of the economic importance of analytics correlates with their foregoing described developments. *Fig. 1.4.1* and *1.4.2* do not descibe up-to-date values, but certainly describe the trends of increases. *Fig. 1.4.1* specifically refers to the *on-line* analytics in process control and includes extrapolations (not predictions) for the global market until 2000, based on established data from the years 1990 and 1994. In *Fig. 1.4.2* for the year 1994 the entire analytical instruments market (including separation methods) is itemized according to manufacturers and methods. The data originate from Frost & Sullivan.[7]

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[1] Felix Bloch, Stanford University, Stanford, CA, USA, 1905 (Zurich) – 1983; 1952 Nobel Prize in Physics “for their development of new methods for nuclear magnetic precision measurements and discoveries in connection therewith”. F. Bloch, W.W. Hansen, M. Packard, *Phys. Rev.* **1946**, *69*, 127.

[2] Edward M. Purcell, Harvard University, Cambridge, MA, USA, 1912 – 1997, 1952 Nobel Prize in Physics (cf. footnote 1). E.M. Purcell, H.C. Torrey, R.V. Pound, *Phys. Rev.* **1946**, *69*, 37.

[3] Richard R. Ernst, ETHZ, Zurich, Switzerland, b. 1933; 1991 Nobel Prize in Chemistry “for his contributions to the developments of the methodology of high resolution nuclear magnetic resonance (NMR) spectroscopy”.

[4] Kurt Wüthrich, ETHZ, Zurich, Switzerland, and Scripps Research Institute, La Jolla, CA, USA, b. 1938; 2002 Nobel Prize in Chemistry “for his development of nuclear magnetic resonance spectroscopy for determining the three-dimensional structure of biological macromolecules in solution”.

[5] Paul C. Lauterbur, University of Illinois, Urbana, IL, USA, 1929 – 2007; 2003 Nobel Prize in Physiology or Medicine “for their discoveries concerning magnetic resonance imaging”.

[6] Sir Peter Mansfield, University of Nottingham, Nottingham, UK, b. 1933; 2003 Nobel Prize in Physiology or Medicine (cf. footnote 5).

[7] See *Chemische Rundschau* **1995**, *11* and *16*.

Information on the latest data and trends can be ordered against "good payment" (in the order of magnitude of some 10^3\$) for example from Frost & Sullivan (www.frost.com/prod/servlet/frost-home.pag). Market analyses of this kind are indispensable for the foundation of a new business venture or for the launch of research projects.

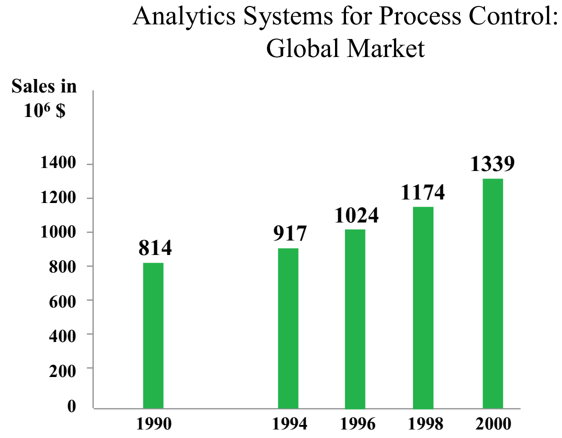

Fig. 1.4.1. Volume of Sales of Instruments for on-line *Process Control on the Global Market (1990 – 2000)*

Some additional data complement the economic aspects of analytical methods. At the beginning of the 1990s the Swiss gross national product accounted for ca. 220 Mrd. CHF, with contributions from agriculture of ca. 4 and the banking sector of ca. 10 %. The contribution of analytics – including chemical industry, comestible goods, academia, medical institutions, research at academia, environmental protection, toxicology, forensics, and archeology (in the sense of conservation of objects of art and authentication) – had been estimated to account for ca. 9 Mrd. CHF (i.e. of the order of magnitude of the contribution of agriculture of ca. 4 %).[1]

In 2000 for 1995 the following data were published as the result of a commissioned study (1996) for the DTI (**D**epartment of **T**rade & **I**ndustry, England):[2] the total amount of analytics in the gross national product of the English economy amounted to 7 Billion pounds, corresponding to ca. 1%.[3] Recently, under the rubric market analysis for 2004, the analytical network *analytica-world* published a worldwide volume of sales of the German analytics sector of 4.3 Mrd. Euro including extrapolations for 2005.[4] Even without actual figures, which are available only to a limited extent, from the above data the significant market volume of analytics is very evident.

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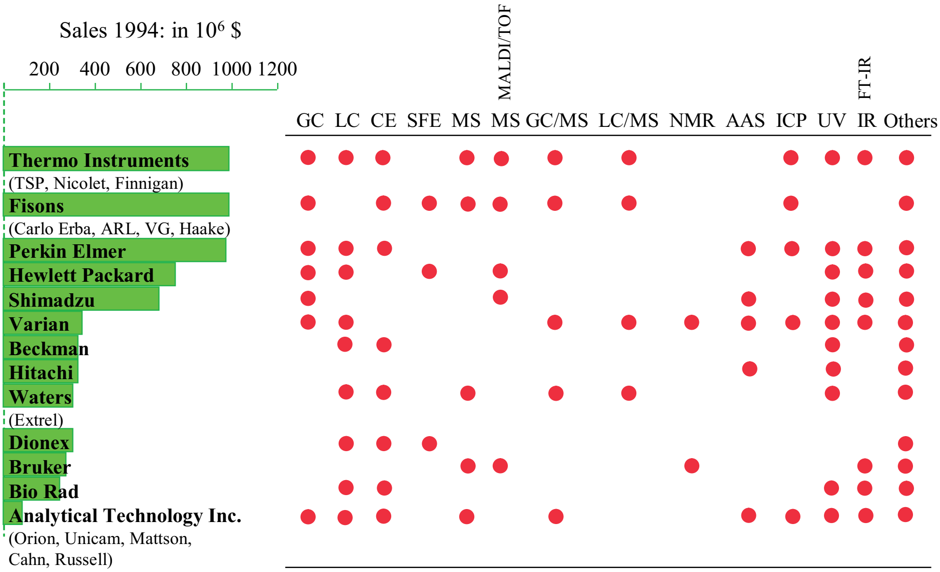
1. H.M. Widmer, *Chimia* **1990**, *44*, 298.
2. B. Perry, J. Ray, *Chem. Industry* (London) **2000**, *15*, 495.
3. According to American nomenclature 1 Billion = 1 Mrd. = 10^3 Mill. (cf. also *Tab. 3*, p.320).
4. www.analytica-world.com/id/38277 (date: 2005-05-27).



	GC	LC	CE	SFE	MS	MALDI/TOF MS	GC/MS	LC/MS	NMR	AAS	ICP	UV	FT-IR IR	Others
Thermo Instruments (TSP, Nicolet, Finnigan)	●	●	●		●	●	●	●			●	●	●	●
Fisons (Carlo Erba, ARL, VG, Haake)	●		●	●	●	●	●	●			●			●
Perkin Elmer	●	●	●							●	●	●	●	●
Hewlett Packard	●	●		●		●						●	●	●
Shimadzu	●					●				●		●	●	●
Varian	●	●					●	●	●	●	●	●	●	●
Beckman		●	●									●		●
Hitachi										●		●		●
Waters (Extrel)		●	●		●		●	●				●		●
Dionex		●	●	●										●
Bruker					●	●			●				●	●
Bio Rad		●	●									●	●	●
Analytical Technology Inc. (Orion, Unicam, Mattson, Cahn, Russell)	●	●	●		●		●			●	●	●	●	●

Fig. 1.4.2. World Market of Instruments according to Sales, Manufacturers and Analytical Methods (1994)

1.5 On the Conception of the Book

The spectroscopic methods described in this book have in common the interactions of different sized molecules with specific wavelength ranges of the electromagnetic spectrum. Interactions mean absorption of energy from a particular spectral region. The discussed wavelength or respective frequency ranges (cf. Chapt. 2.1, p.15) are: the UV and visible region, the near Infrared, the Infrared, the ESR and the NMR region. The basic physical principles of these interactions with the “light” in these spectral regions together with all deducible consequences constitute the structure of this book as an unbroken thread. The conventional view of spectral regions, i.e. of the spectroscopic methods, is replaced by the view of physical phenomena, by which these spectroscopic methods are interrelated. The interactions of molecules within the particular spectral regions affect very different elements of molecular structure: valence electrons, bonds between atoms, the nuclear spins of atoms or the spins of electrons. Besides the principal similarities these interactions mean as well differencies between the spectroscopic methods with important consequences. These aspects are the central themes of Chapters 3 and 4.

In Chapter 2 I describe the electromagnetic spectrum, including some comments on the developments (state of technology, costs etc.) of the available instruments, particularly with regard to NMR spectroscopy. To aid in the understanding of these aspects prior reading of the central Chapters 3 and 4 is advised.

Chapter 5 addresses the various different methods and results of spectroscopy of analytes in the four phases (from gas to solid state). Chapter 5.5 (p. 157) inter alia concerns an often neglected item: the preparation of analytes. Their concentrations must be adjusted to the sensitivity of the respective analytical method. Also there is the principal issue of whether the analyte should be analyzed in the solid or in the liquid (mostly in solution) state. This question concerns not only NMR spectroscopy but all spectral regions. Chapter 5.4 (p.139) primarily is devoted to solid-state NMR spectroscopy and how the results differ from those of NMR of solutions. In NMR and ESR spectroscopy the effects of phase of the analyte are particularly distinctive. As for the optical regions of the electromagnetic spectrum (UV to IR) the nature of the problem should define the phase of the analyte for the analysis.

Chapter 6 addresses the differences between the classical CW (**C**ontinuous **W**ave) and FT (**F**ourier **T**ransform) spectroscopy. The transition from CW to FT spectroscopy is an immediate outcome of the development of computer technologies (described in Chapter 1.3, p. 6). Without fast computers the FT technique would not be available and ESR and NMR spectroscopy would not have achieved their relevance today. The same applies to all multidimensional spectroscopies in the optical (UV/Vis to IR) as well as in the resonance region (ESR and NMR) and for time requirements (e.g. in process control) of optical methods on the time scale of seconds.

In Chapter 7 important aspects of the two- and three-dimensional (2D, 3D) methods are discussed. For the nonspectroscopist at first view the term 2D spectroscopy is incomprehensible, since spectra as “images” of absorption processes always are two-dimensional. Chapter 7 will clarify this point.

Chapter 8 describes the application ranges, the importance and the limits of the individual spectroscopic methods. Since even at the absolute zero point on the thermodynamic temperature scale (0 Kelvin K or -273.15 °C) all molecules are still flexible, we also have to consider the dynamic aspects of spectroscopic methods (Chapt. 8.3, p. 284). Besides structure analyses (Chapt. 8.1, p. 208) concentration and kinetic measurements constitute a wide application range (Chapt. 8.2, p. 270). The physical and therefore measurement basis for the determination of diffusion constants is also the basis for imaging ESR and NMR spectroscopy (Chapt. 8.4, p. 293). The terms opt(r)odes and sensors refer to a perfected, mainly automated analysis, for example in process control. Tandem or combined methods have been briefly characterized already in Chapters 1.1 and 1.3. The application of sensors i.a. is linked to tandem methods (Chapt. 8.5, p. 304). Chapter 8.6 (Chemometry, p. 307) is a short description of statistical computer-aided evaluations of analytical data and their applications.

Chapter 9 addresses the conventions of the communication of spectroscopic data, which ensure the compatibility of data from various origins.

Concluding with Chapter 10 I have collocated a selection of textbooks from the spectroscopic literature as well as my personal favorite books. Aside a few exceptions I do not cite scientific original papers.[1] By nature these exceptions are selected subjectively and predominantly concern prominent physical and spectroscopic developments.

In the Addendum the reader finds Tables with conversion factors, constants etc. Wherever in the text, in Tables or in Figures numerical values are quoted, they originate from standard works on the particular methods.

Investigating molecules by means of the discussed spectroscopic methods, each of them delivers a specific insight into the structure and the properties of these molecules. The summation of all information eventually yields an overall picture, which allows for the understanding of the properties of these molecules. My description of the various spectroscopies in this book should also be understood in this sense. The sum of the individual Chapters should provide an overall picture of the spectroscopies, which concern the *reversible* absorption of energy from the electromagnetic spectrum.

Within Chapters 3 and 4, which describe the physical phenomena of spectroscopic processes, the individual spectral regions – to aid navigation by the reader – are discussed in terms of decreasing energies of the absorbed electromagnetic radiation (from UV through IR up to NMR spectroscopy) and are compared with each other. Therefore, Chapters 3 and 4 are structured into five Subchapters finishing with Subchapters 3.5 and 4.5 containing comparative summaries.

Chapter 6 on CW and FT measurement techniques and Chapter 7 on two- and three-dimensional (2D and 3D) spectroscopies primarily are based on NMR spectroscopy with cross references to the other spectroscopic methods. Particularly the description of two- and three-dimensional spectroscopies within this book for nonspectroscopists has been a challenge. Since their discription cannot be missing from a book on modern spectroscopies, I have attempted to describe their physical basis in an elementary, comprehensible and condensed form.

I have described the themes in all Chapters with the ambition, that each Chapter alone provides the essential information for its specific comprehension. Numerous cross references assure the conjunctions between the physical interrelations.

Readers, who want to concentrate on the physical principles and interrelations, can confine themselves to Chapters 2 to 4. It is one of the benefits of the presentation in hand, that individual requirements for information allow for the extent of occupation with the themes of this book. The reading of Chapters 2 to 4 can be amended – according to information demands – by the reading of Chapters 1 and 5, and 6 to 9. For the reader skilled in one or the other spectroscopy the two Subchapters 3.5 and 4.5 are particularly informative. And another aspect of the presentation of the themes in this book: I have discriminated supplementary information from the fundamental physical interrelations by fine print or footnotes (quasi

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[1] On the one hand these are to be found in the cited books and on the other hand are accessible in industry and in academia from online databases: e.g. *SciFinder*, American Chemical Society (scifinder.cas.org) or *reaxys* (www.reaxys.com). For some short additional information see www.infochembio.ethz.ch/en/db.html.

a distinction of *important to know* from *nice to know*). Naturally this distinction is a subjective one. The in Chapter 10.2 cited compendium *Essential NMR* of Bernhard Blümich allows a similar selection between independent Chapters on NMR spectroscopy and its applications. Apart from this compendium to my knowledge two other books in the documented literature to some extent pursue a similar concept. In the first one[1] however the focus is, as the subtitle shows, a predominantly technical one. In the second book, meanwhile ca. 35 years old, the authors partly follow an analogous concept, in as far as the methodical collocation of the spectroscopies is not entirely consequent and is mingled with application-oriented Chapters and some on categories of compounds (i.e. the book of Pierre Laszlo and Peter Stang in Chapt.10.2).

Finally, a concluding comment to all data specified in this book (for instance bond lengths, electronegativities, coupling constants, or relaxation times): In contrast to the rightly strict scientific practice I have abandoned the citation of the origins of the data. The wide range of the book and its limited volume requires this. All data originate from the books mentioned in Chapter 10 and the original papers cited in those, and as well are to be found in the above named databases (footnotes 1, p.13 and 43).

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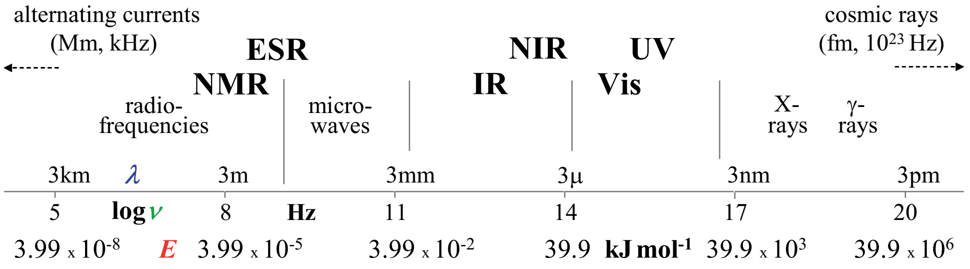
[1] D.W. Ball, *The Basics of Spectroscopy, Tutorial Texts in Optical Engineering*, Vol. TT49; Arthur R. Weeks, Jr. (Ser. Ed.), SPIE PRESS, Bellingham, Washington, **2001**.

2 The Electromagnetic Spectrum

2.1 Its Regions and Present-Day Comprehension

As *Fig. 2.1.1* shows, the electromagnetic spectrum ranges from cosmic rays (mainly protons) at the short-wave side in the **f**emto**m**eter-range (fm, 10^{-15} m, 10^{23} Hz) to the alternating current region at the long-wave side in the **m**ega**m**eter-range (Mm, 10^{6} m, 10^{3} Hz). Between these boundaries there lie *i.a.* the regions of γ-rays (from nuclear transformations and reactions), of X-rays (or Röntgen-rays, see *Tab. 6*, footnote b, p. 322) of different energies, of the terahertz-rays (THz, 10^{12} Hz, very long-wave heat radiation), as well as the microwave and radio frequency regions. The UV/Vis, NIR and IR regions in the nm- to mm-range follow one another directly. The ESR and NMR regions are located in the cm- and m-range of the electromagnetic spectrum.



$$\boxed{E = h\nu = hc/\lambda}$$

E = energy, ν = frequency and λ = wavelength of photons
h = Planck constant, c = speed of light

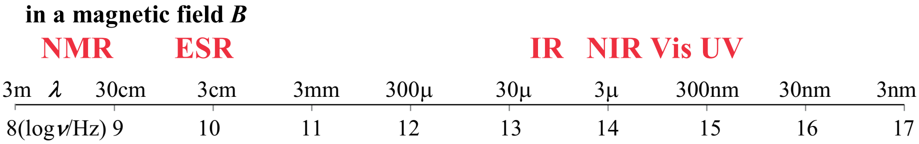
Fig. 2.1.1. The Electromagnetic Spectrum at a Glance

As a result of reactions with and absorptions by the protective atmosphere predominantly the relatively lower-energy, longer-wave range of the spectrum from ca. 200 nm arrives on our earth. The short-wave UV-region, in particular the UV-C (< 290 nm) and partly the UV-B (ca. 290 to 320 nm), is absorbed by the gas ozone (O_3) in the atmosphere. In the context of the so-called ozone holes this is wellknown. These holes result from degradation of the ozone (with formation of oxygen, O_2) in its reactions with photolytically (i.e. by catalytic photons of the solar radiation) accumulated radicals. These radicals are products of our partly substantially reduced industrial emissions, such as for example the **c**hloro**f**luoro**c**arbons (CFC, e.g. from cooling aggregates), CO_2 (combustion of carbonic energy sources), or methane (*i.a.* from agriculture). In contrast UV-A (ca. 320 to 400 nm, together with UV-B) is essential on the one hand for the generation of vitamin D, but on the other hand it causes sunburn (actinic dermatitis) and affects the eye.

The relation $E = h\nu$ links the energy E of a photon γ of the electromagnetic radiation with its frequency ν via the Planck constant h. Its wavelength λ and the frequency ν are inversely proportional via $\nu = c/\lambda$ to the speed of light c. The reciprocal proportionality between λ and

ν defines the connectivity of the three scale values λ, ν, and E in *Fig. 2.1.1*. The energies of the electromagnetic radiation span a range of ca. 20 powers of ten. The Bohr[1] frequency condition E (or ΔE) = $h\nu$ states, that energy will be absorbed by a molecule, whenever the energy gap ΔE between two states of this molecule satisfies the frequency condition. Hence during registration of a spectrum all transitions between molecular states will be excited, of which ΔE values fulfill this condition. By selection of the spectral region we select the nature of transitions between molecular states. In *Fig. 2.1.2*, which defines the relevant sections of the electromagnetic spectrum for the spectroscopic methods in this book, the common measuring range is specified for each of these (IR, NIR, Vis, UV), except for ESR and NMR.[2] But for all of the methods a characteristic ΔE with the corresponding frequencies (in Hz), wavenumbers (in cm^{-1}), or wavelength (in λ) is specified.[3]

IR: 2.5 – 20 µ (5000 – 500 cm^{-1}) $\tilde{\nu} = \nu' = 1/\lambda$ (cm^{-1})
NIR: 780 – 2500 nm (0.78 – 2.5 µ)
Vis: 420 – 780 nm
UV: 200 – 420 nm



$$\boxed{\Delta E = h\nu = hc/\lambda}$$

$N_A = 6.022 \times 10^{23}$ mol^{-1}
$h = 6.626 \times 10^{-34}$ J s
$c_0 = 2.998 \times 10^{8}$ m s^{-1}

	ΔE in kJ mol^{-1}
^{1}H-NMR, 900 MHz:	3.591×10^{-4}
ESR, 9 GHz:	3.591×10^{-3}
IR, 2000 cm^{-1}:	23.965
NIR, 1000 nm:	119.626
Vis, 500 nm:	239.652
UV, 300 nm:	398.752

Fig. 2.1.2. The Electromagnetic Spectrum (NMR to UV) and typical ΔE Values

The fundamental condition $E = h\nu$ is one of the results of the revolutionary development of physics at the turn to and beginning of the 20th century. This period spans a few decades and its description does not pertain to the objectives of this book. However, understanding spectroscopy requires a short outline of the principal aspects of this development. Reduced to the essentials it is a matter of the awareness that the classical laws of macroscopic physics do not suffice to explain the experimental observations in atomic and nuclear dimen-

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[1] See Footnote 1, p.19.

[2] In the literature the definition of these "common" measuring ranges is not at all consistant and not least a spectrometer-specific value. Nevertheless, the differences are negligible regarding the principal aspects.

[3] The values in kJ mol^{-1} result from the Bohr frequency condition by multiplication of ΔE with the Avogadro constant N_A (see also p. 20 and 31).

sions, for example the properties of elementary particles (such as electrons e, protons p, or photons γ). The investigations into the nature of electromagnetic radiation were even the starting point for the insight: the properties of elementary particles can only be described entirely by the assumtion of a duality. They have in a complementary sense wave as well as particle character. Photons γ have the energy $E = h\nu$, which is the product of their frequency ν and the Planck constant h (see footnote 2, p.18). The latter implies that the electromagnetic radiation is not a continuum, but consists of so-called light quanta, i.e. photons with discrete energies (quantum: Latin, meaning indivisible). Furthermore, it follows as well that atoms and therefore all molecules exist in discrete energy states only. These discrete states of molecules are the premise and basis for the information content of spectroscopic methods. A continuum would not provide any information. h quantizes (divides) the energy states of matter and light energy into the smallest possible amounts.

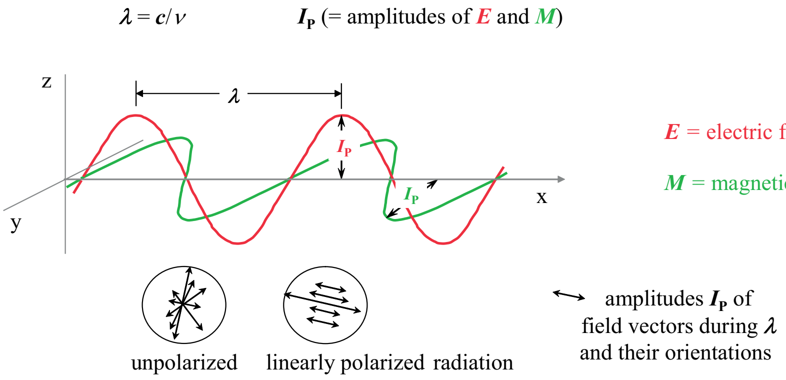

Fig. 2.1.3. Quantities of the Electromagnetic Radiation and its Linear Polarization in z

Understanding the absorption of photons – in the optical (UV/Vis to IR) as well as in the resonance region (ESR, NMR) – requires knowledge of the electric and magnetic field of the electromagnetic radiation. The vectors of both fields oscillate (Latin, vibrate or swing) with the frequency ν perpendicularly to each other and to the propagation direction in x with the speed of light c. Polarizers[1] transform natural unpolarized radiation, in which all orientations of field vectors are present, into linearly polarized radiation, in which the vectors oscillate only in one direction. *Fig. 2.1.3* displays the field vectors of E (in z) and M (in y) in linearly polarized form. The amplitudes I_p of E and M define the intensities I_P of the radiation as a function of the number of photons/s.[2] The field vectors of E and M each are the product of two counter-rotating vector components. Hence linearly polarized radiation can be looked at as superposition of two circular polarized waves. The relative phase of the two waves de-

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[1] They make use of different phenomena such as e.g. absorption, reflexion, birefringence, and interference of the electromagnetic radiation.

[2] Macroscopically measured as I_e in W or J s^{-1}.

termines the position of the polarization plane. Optically active (or chiral) molecules turn the polarization plane of linearly polarized light via phase shifts as a result of different propagation speeds of the two circularly polarized waves (*Fig. 2.1.4*).

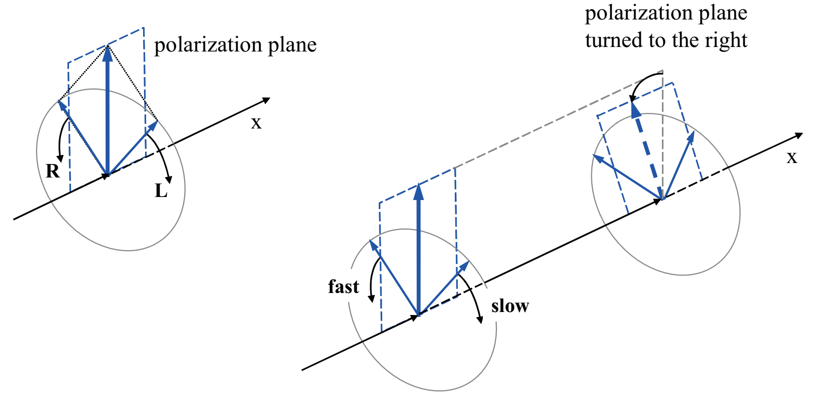

Fig. 2.1.4. Left (L) and Right (R) Polarization of the Electromagnetic Radiation

In the optical region a precondition for the absorption of photons is the parallel oscillation of the vector of *E* (or one of the counter-rotating vector components) to the vibration direction of the respective vector of the molecular response (see Chapt. 3.1 and 3.2, p.33 and 42). Analogues are valid in the resonance region for one of the counter-rotating vector components of the magnetic field *M* (see Chapt. 3.3 and 3.4, p. 50 and 59).

The terms quantum theory, quantum physics, or mechanics are used frequently and synonymously, but they always implicate the aspect of the discrete noncontinuous states of matter. The very new term quantum biology carries this perspective over to the science of biological macromolecular complex systems. The completion of classical physics by quantum physics is bound to names such as A. Einstein,[1] M. Planck,[2] P.R. de Broglie[3], W. Heisenberg[4] (1925, quantum mechanics), and E. Schrödinger[5] (1926, wave mechanics).

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[1] Albert Einstein, Kaiser-Wilhelm-Institut (now Max-Planck-Institut) für Physik, Berlin, 1879 (BRD) – 1955; 1921 Nobel Prize in Physics "for his services to Theoretical Physics, and especially for his discovery of the law of the photoelectric effect".

[2] Max K.E.L. Planck, Universität Berlin, 1858 – 1947; 1918 Nobel Prize in Physics "in recognition of the services he rendered to the advancement of Physics by his discovery of energy quanta".

[3] Pierre R. de Broglie (Prince Louis-Victor), Sorbonne University, Paris, 1892 – 1987; 1929 Nobel Prize in Physics "for his discovery of the wave nature of electrons".

[4] Werner K. Heisenberg, Universität Leipzig, 1901 – 1976; 1932 Nobel Prize in Physics "for the creation of quantum mechanics, the application of which has, inter alia, led to the discovery of the allotropic forms of hydrogen".

[5] Erwin Schrödinger, Universität Berlin, 1887 (Austria) – 1961; 1933 Nobel Prize in Physics (with Paul A.M. Dirac) "for the discovery of new productive forms of atomic theory".