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Chemometrics

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INTRODUCTION

Chemometrics is the discipline concerned with the application of statistical and mathematical methods, as well as those methods based on mathematical logic, to chemistry. This review, the eighth of the series, and the sixth with the title "Chemometrics", covers the more significant developments in the field from December 1987 to November 1989. The format follows approximately that of the previous review (1), the one first used by Delaney (2) in 1984.

The volume of literature concerned with mathematical, statistical, and logical methods for analyzing chemical data is a clear indication that the field is healthy. The distribution of articles comprising the literature of chemometrics indicates several trends. One is the presence of slow but steady growth in the number of workers publishing in the field. The other is the rapid growth of chemometrically oriented articles published in journals outside of pure chemistry. Workers in many areas of applied chemistry, from those interested in medicine to those concerned with materials processing, to name but a few areas where interesting work appeared, have embraced chemometric methods and are publishing their successes. The number of articles concerned with application of chemometric methods now exceeds by far those aimed at development of new chemometric methods. This situation, along with the need to conserve journal space, forces some additional selectivity in this review of the field. As before (1), emphasis will be placed on work concerned with analytical chemometrics. In this review, discussion will be further limited to work that either reviews some aspect of the field or work presenting novel chemometric methods. Routine application of chemometrics will, in general, not receive mention because of the volume of work being published.

A third trend in the literature of chemometrics can best be seen in a comparison. In 1980, Kowalski (3) listed the results of computer searches of *Chemical Abstracts* for key words pertinent to chemometrics. Some of the references he recovered in the search were not germane, but the vast majority were useful in producing the fundamental review. These same key words, when used in computer searches over the period January 1988 to December 1989 produced some surprisingly changes. Table I summarizes the results. The numbers of

articles detected from the keyword searches listed certainly do not support a large growth in the literature of chemometrics. Instead, corrected for the differences in the time periods over which the searches were conducted, they might even suggest a decline in activity. But, as those familiar with chemometrics might suspect, these search statistics are somewhat deceptive. Simply inspecting the articles detected in the search demonstrates that most (about 75%) of the publications detected during the 1989 search are applications of chemometric methods and most occurred in journals documenting fields far removed from pure chemistry. Very few of the publications detected in the search were concerned with development of novel chemometrics. In particular, publications from the two chemometrics journals were only infrequently detected in the search. In general, these publications—particularly those in well-established areas of chemometric research—were associated with such specific and narrowly defined key words that a broad search of the sort listed in Table I was not useful in identifying them. Those publications where the whole idea of chemometrics was novel were the ones most likely to be associated with key words of the sort given above, and these were most often detected in the search. To ensure that the bulk of relevant literature was properly considered in the preparation of this review, the electronic searches were combined with hand searches of the journals where most of the new work in chemometrics appears. Hand searches located about 20% of the total number of articles, about the same fraction as observed in the previous review (1). Hand selection was applied to the approximately 5000 references resulting from the selective computer and hand searches to determine the final list of references for the review. Comparison between the two periods examined above is therefore difficult because it seems that the field of chemometrics has become much more sophisticated and specific, while the range of applications of chemometrics has widened greatly. Perhaps the change in the nature of chemometric articles detected by a search using broadly defined keywords reflects a maturation of the field.

The results summarized above also indicate a need for considerable forethought if one will be relying on a computer search to learn of new work in fundamental chemometrics.

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The search using those key words summarized above was combined with more specific searches, using sets of specific key words, to obtain a list of papers published in the field over the past 2 years. Even with these more specific sets of key words, however, a large amount of material was detected that was not relevant to the review, but, more significantly, a large number of relevant material was not detected at all. Unfortunately, hand searches are becoming less and less feasible as the number of journals—and their cost—increases. Few will have ready access to all relevant material, making the electronic search the method of choice, at least when compared to a hand search of *Chemical Abstracts*. Sadly, the improvements in the field that occurred during the past 2 years do not include substantial advances in the efficiency of electronic searches for chemometrics literature. With the ever-increasing amount of literature in this field, the need for careful selection of keywords and prompt indexing of publications has become even more important. Editors and authors are urged to bear these trends in mind upon publication of work in chemometrics.

It would indeed appear that the field of chemometrics has begun to change. The innovators in the field are no longer responsible for the majority of the work appearing in print. Increasingly, data analysis is becoming something that is expected of those hoping to publish work in areas of measurement chemistry, and chemometric tools are now seen by many as necessary aids to that data analysis. With the decreased rate of innovation in development of measurement hardware coupled with the increased rate of innovation in development of user-friendly software, the access to chemometric methods grows easier every day. While this change speaks well for the continued health of the field, there is now a similarly increasing need to educate the increasing base of new users of chemometrics in addition to continuing to advance the field. The chemometrics short courses, symposia, recently published texts, and tutorials in chemometrics journals (and elsewhere) remain important ways to continue this process.

Given the relatively small number of formal courses in chemometrics at the undergraduate or postgraduate levels, education remains very important to the continued growth of the field. Fortunately, education is an area where notable changes have taken place over the past 2 years. One aspect of education is the introduction of new users to the field. The substantial increase of tutorial articles in user-oriented journals (see below) that occurred over the past 2 years should do much to spread chemometric concepts. A few of these tutorials are not in the traditional style. Bruce Kowalski has prepared two 40-min videotapes, one offering a broad overview on chemometrics and the other introducing multivariate calibration methods. The use of videotape to introduce chemometrics is an interesting approach, in that a little of the feeling of a "live" lecture comes across to the viewer. This effect breathes a little life into what might be an otherwise dry subject for some.

Improving and extending the skills of those already familiar with basic chemometrics is another aspect of chemometrics education. In this area, the short course appears to be the educational instrument of choice. During the past 2 years, the number of short courses in chemometrics has increased

Table I. Computer Search of Chemical Abstracts over Two Periods: January 1976–October 1979 and January 1988–December 1989

key word	no. of CAS entries detected in search	
	1/76–10/79	1/88–12/89
calibration	2312	941
chemometrics	8	68
sampling theory	2	1
multivariate analysis	52	59
parameter estimation	68	46
time series analysis	20	4
spectral analysis	1102	225
optimal control	119	39
systems analysis	80	22
evolutionary operation	1	2
operations research	6	0
regression	912	379
mathematical analysis	116	26
statistics	2072	2872
pattern recognition	232	46
data reduction	70	27
experimental design	266	56
curve fitting	120	42
spectral resolution	27	14
deconvolution	133	142
factor analysis	175	84
principal components	46	94
feature selection	8	2
Fourier transform	34	1359
information theory	227	35
signal processing	44	76
peak fitting	6	3
digital filtering	4	11
least squares	315	143
nonlinear regression	30	24
nonparametric statistics	1	10
simplex	27	984
nonlinear calibration	7	3
multiple regression	61	16
multivariate calibration		21
multivariate prediction		1
artificial intelligence		83
partial least squares		29
image analysis		3
expert systems		119

substantially. A few of the many courses are listed here, since many of these short courses are offered on a continuing basis. The European Spring School in Chemometrics, a 5-day short course, was held in England in spring 1988 and 1989. The European School on Chemometrics was held in Spain, in summer 1989. Other multiday short courses in chemometrics were given in Spain, Ecuador, England, Sweden, Austria, and Poland. Shorter chemometrics short courses, lasting a day or less, were offered in Finland and at the Scientific Computing and Automation Conference and FACSS Conferences in the U.S.

During the period covered by this review, there were several international meetings where presentations on chemometrics were a major component. Among them were CAC IV (Chemometrics in Analytical Chemistry), held in Amsterdam. Papers from that conference were published in a special issue of *Analytica Chimica Acta*. The Conference for Mathematics in Chemistry, held in College Station, TX, in November 1989, was a meeting with a varied and interesting program, with speakers from chemometrics, statistics, applied mathematics, engineering, physics, and traditional areas of chemistry. Papers from this conference will be published in a special issue of *Chemometrics and Intelligent Laboratory Systems*. The Second Snowbird Conference on Computer-Enhanced Spectroscopy was published as a book, *Computer-Enhanced Spectroscopy*, edited by Henk Meuzelaar. Other conferences that were published include the Colloquium Chemometricum Mediterraneum, held in Barcelona, and published as a special issue of the *Journal of Chemometrics*, and the Meeting on Expert Systems in Chemistry and Chemical Industry, held

in London and published in *Chemometrics and Intelligent Laboratory Systems*. The same Journal will also publish the proceedings from the First Scandinavian Symposium on Chemometrics, held in Lappeenranta, Finland, in October 1988, and the Symposium on Chemometrics and Intelligent Automation at the CIC Conference, held in Victoria, Canada, in June 1989. Finally, a special issue of *Mikrochimica Acta* was devoted to papers on chemometrics presented at the Fourth Conference on Computer-Based Methods in Analytical Chemistry (COBAC IV). Three other publications also offered special issues with papers on chemometrics. In one, papers presented at a chemometrics symposium at the 1986 Pittsburgh Conference, held in Atlantic City, appeared in a special issue of *Trends in Analytical Chemistry*. The other covered papers given at the Conference on Accuracy in Trace Analysis, held at the U.S. National Bureau of Standards. These papers, including two plenary lectures and two sessions with invited papers in chemometrics, are published in the *Journal of Research of the National Bureau of Standards*. Other major meetings were the EUCHEM Conference, held in Trieste, in summer 1988, and the yearly CAC, EAS, and FACSS meetings in the United States, all of which had sizable symposia on chemometrics.

Meetings scheduled for the coming 2-year period include COBAC V, to be held in Vienna, the Second EPA Conference on Progress in Chemometrics, to be held in Las Vegas, and the Third Conference on Computer-Enhanced Spectroscopy, to be held in Snowbird, UT, all in 1990. There also will be sessions on chemometrics at the Pittsburgh Conference, the FACSS meeting, and the Eastern Analytical Symposium. Sessions on chemometrics are also scheduled for the Gordon Research Conferences on Statistics in Chemistry and Chemical Engineering and on Analytical Chemistry. In 1990, both of these conferences offer especially strong coverage of areas that will be of interest to those in chemometrics. Other upcoming meetings can be found in the journal *Chemometrics and Intelligent Laboratory Systems*, which routinely publishes notices and calls for papers.

The fundamental review (1) continues to be the most complete overview of the field. Other than Brereton's review (4), published late in 1987, no other attempts at comprehensive coverage of chemometrics have appeared during the past 2 years. Brief overviews of chemometrics were given by Meglen (5) and Kowalski (6). Description of chemometrics research, by regions, were given for Europe by Wegscheider (7) and for China by Chen (8). Other summaries have been provided in the "News" section of *Chemometrics and Intelligent Laboratory Systems*.

Historical overviews of selected aspects of the field have also appeared. Savitzky recounted his collaboration with Golay for research on polynomial smoothing (9), and Geladi provided an overview of the development of the partial least squares (PLS) algorithm (10). Cooley discussed the history of the fast Fourier transform and his "rediscovery" (with Tukey) of the fast transform algorithm that bears their names (11).

BOOKS, SOFTWARE, AND TUTORIALS

Books. The high rate of publication of specialist books on chemometrics that was the hallmark of the previous review period has slowed somewhat during the past 2 years. Some decrease is to be expected, given the large number of texts introduced in 1986-88. The book with the largest impact on the field of chemometrics during this period is not even in the field of chemistry, at least not in the traditional sense. *Numerical Recipes* (12), a book by four physicists, covers many routine and not-so-routine computational tasks which will be of interest in chemometrics. This unique book, which offers excellent discussions of the theory of numerical methods as well as solid code in the FORTRAN and PASCAL languages, was sold out upon publication in 1986 and only recently has become readily available again. Its immediate and frequent citation among references is one tribute to its popularity with those in chemometrics. Another is the emergence of chemometric methods based on numerical procedures (e.g., simulated annealing optimization), which were lucidly presented in its pages. Books that will be of more specific interest to those in chemometrics include ones on correlation analysis of chemical data (13) and topological methods in chemistry (14). The proceedings of the Second Snowbird Conference

described above have also appeared in book form (15). Recently, Martens and Naes have published a new text on multivariate calibration methods in chemometrics (16). This book's unusual illustrations, combined with its nice, balanced presentation of theory and results, are sure to make it popular. Three books concerned with teaching computational skills in chemistry appeared during the period. Zupan's text *Algorithms for Chemists* is a structured introduction to good programming, which at the same time teaches key details in translating multivariate methods to working code, not to mention a little chemometrics (17). Johnson's text on computational chemistry (18) offers an introduction to the use of computers for calculations in chemistry, with examples in the Basic language. Ebert et al. (19) also offer an introductory text, but one aimed at those teaching themselves. Their book covers application of computers to problems in chemistry and related fields, and it includes diskettes with programs in Basic and PASCAL.

The statistical side of analytical chemistry also received considerable attention during the period. Miller and Miller's introduction to statistical concepts in analytical chemistry came out in a second edition (20). Lloyd Currie has edited a new book concerned with detection in analytical chemistry (21), and John Taylor published a monograph on quality assurance, in which he covered statistical methods for sampling, calibration, and validation of scientific data (22). There was also a significant increase in the number of statistics books published, many of which should be of interest to those in chemometrics. Coleman and Van Loan published a very valuable handbook on matrix computation (23). This book provides a basic introduction to the LINPACK function set and to the BLAS operations for linear algebra in the FORTRAN and MATLAB languages. Two new books appeared on nonlinear regression methods (24, 25), and books treating experimental design (26), stochastic systems (27), and principal component theory (28) were also published. Finally, an interesting text on time series analysis appeared (29); this text is accompanied by software which sets up a complete programming environment for time series analysis on the IBM-PC or compatibles. For those interested in learning more about neural networks, Pao's new book (30) offers an introduction to the field from the perspective of pattern recognition and fuzzy sets.

Programming remains an important part of chemometrics. It is in this area that some of the most profound changes are occurring in chemometrics. Despite those changes, some traditions remain. One is the Basic programming language. Those interested in Basic programming will find the new collection of subroutines for scientific computing (31) useful, and Cooper (32) has provided an introduction to Basic programming that goes well beyond the usual presentations previously available from other authors. Other languages, especially structured languages such as PASCAL or C, offer many advantages over the older, more limited Basic language, but the wealth of application packages that exist for Basic or FORTRAN are not yet commonly available. That unhappy situation is slowly changing. C language programmers will appreciate the set of numerical functions from Baker (33), who provided a tested C code for all sorts of numerical methods. There will soon be a version of *Numerical Recipes* in C as well. For some tasks, even powerful languages like C cannot handle the burden. One example is in the manipulation of analytic expressions. Recent interest in computing and applied mathematics of analytic functions has been directed to symbolic computation. A symbolic calculation can be as basic as the simplification of an algebraic expression or as complex as the automated generation of numerical experiments and simulations. In either case analytic, not numerical, results are generated. A recent book presented a collection of papers on the application of symbolic computation to applied mathematics and engineering (34). Another book presented a tutorial and a detailed reference for Mathematica, one popular new language for symbolic computing (35). This book is certainly the clearest presentation of symbolic computing, and it will be useful to anyone trying to use symbolic computation, even those using symbolic languages other than Mathematica.

Software. As noted above, the programming of chemometric tasks is entering a new era. Symbolic computation can be used for a number of tasks, from solving simultaneous

equations in a equilibrium to handling complex integrals in quantum mechanics (36). Symbolic computation programs, for example, MACSYMA, are well established. These older programs, usually written in a dialect of Lisp, require a great deal from the resources available on a minicomputer. While the opportunities were there, few chemists investigated symbolic computing. That situation has changed now that less-demanding symbolic processors are available on desk-top platforms. Symbolic computation programs are now available on 640 kbyte IBM-PC-class machines (e.g., Derive) and on the Macintosh (Mathematica, Maple). Some of these programs can also be used to obtain numerical solutions. Mathematica, for example, can be used to perform all the usual calculations on n -dimensional arrays.

Software for logical operations continued to gain in popularity. Not only have languages for artificial intelligence become readily available for IBM-PC-class machines (PROLOG and others), but many predeveloped shells for expert systems have also appeared. Many of these packages are significantly faster and less expensive than those available only 2 years before. Improvements in this software have significantly increased the rate of publication of research concerned with the logical aspects of chemometrics.

Software intended "only" for numeric computation has also undergone major changes. Several new computer languages make it much easier to perform matrix and vector operations than in conventional languages based on scalar operations, such as Basic, FORTRAN 77, or C. The most powerful and most popular of these matrix-based languages is MATLAB, a matrix-based language with a large number of built-in functions for signal processing and linear algebra. A multivariate calibration package (with PLS, principal components regression, and other methods) can be purchased for MATLAB, as well as other modules for control, system identification, and nonlinear modeling. MATLAB takes full advantage of the careful optimization that went into LINPACK and other numerical packages, but it performs matrix-based operations much like APL, and it is both interpreted and compiled, so that programs run rapidly, but the user may also try operations in "immediate" mode, much as in Basic. Unlike APL, programs are written with a PASCAL-like syntax, without the need for special keyboards. Features of MATLAB that make it attractive for chemometrics education and research can be found in the review by O'Haver (37). Other numeric languages include GAUSS (which is much like MATLAB, but with fewer functions and better graphics), Eureka, MathCAD, Mathview, and TK Solver. All of these provide a "programming environment", with graphics, program editors, and so on. At least four major chemometrics research groups in the U.S. are now programming in MATLAB, mainly because it substantially decreases the time needed to try an algorithm.

In addition to these changes in approaches to scientific computing, the flood of new, easy-to-use statistical software for PC-level machines continues unabated. Virtually all of the major packages underwent improvements during the past 2 years to improve efficiency, enhance graphical capabilities, and simplify the user interface. While there are now so many statistical packages that it is impossible to list them all, a few deserve special note. One new package, Prodas, uses matrix mathematics and graphics like the numeric processing languages discussed above, but this package also includes the usual statistical routines offered by other packages. ECHIP is another interesting package which offers a number of powerful methods for experimental designs and response surface mapping. Most of the common mainframe statistical packages can be gotten for an IBM-PC-class machine, including SPSS, BDMP, SAS, and others. It is now far simpler to get results from statistical tests than to decide what statistical tests are to be run and what the results mean, a problem that has been addressed by several expert systems oriented to statistical tests. Two packages that offer expert system capabilities in deciding what tests are needed and what the results of these tests mean are The Statistical Navigator and ESS.

A few packages specifically targeted for the chemometrics market also were announced. New pattern recognition packages were made available for the IBM-PC by Elsevier Scientific Software (PARVUS) and by Infometrix (Ein*Sight v2.5). An add-on package for self-modelling curve resolution

of chromatographic data on data stations from Waters and Hewlett-Packard (Quick-Res) was released by Infometrix. Other chemometrics packages designed to add on to base software were released by Spectra-Calc and by Mathworks. Both emphasized multivariate calibration methods, including partial least squares. Many instrument vendors now also offer multivariate calibration packages for spectrometric equipment, either as part of the base system or as an add-on package.

User-developed programs also continue to be published, but most are now bundled with some set of applications which represent the main thrust of the work. Papers of this sort will be discussed in the sections below, where appropriate. Papers concerned only with development of software are much less common now, and it has become rare for the full source code listing to be published in chemometrics, in part because of the increasing sophistication (and length!) of user-supplied software. The chemometrics journals now offer reviews of commercial software as opposed to articles reporting new software, with listings of the source code; only the journal *Trends in Analytical Chemistry* has continued regular publication of source code. Among the software listed there was a program for analysis of variance for model validation (38). During the review period papers appeared on the multivariate program UNSCRAMBLER (39), a general software package for multivariate calibration and prediction, and another multivariate classification and calibration program (40). The SimuSolv package for building and solving models containing differential equations was also reported (41). Graph theory and reverse library searching are used in TOX-MATCH and PHARM-MATCH software for prediction of toxicological of pharmacological features of a test compound (42).

Tutorials. In the last review, a need for clearly written tutorial articles on selected aspects of chemometrics was noted (1). Over the past 2 years the number of tutorial papers, both on the details of chemometric methods and on applications of chemometric methods, increased dramatically. Many of these concerned the statistical side of chemometrics. Miller and Miller introduced statistical techniques for evaluation of error in analytical experiments (43). Taylor discussed the role of statistical methods in quality assurance (44) and the need for planning and experimental design to obtain high-quality analytical data from a set of experiments (45). The principles of sampling were discussed from a theoretical standpoint by Kateman (46) and from a more conceptual viewpoint by Springer and McClure (47). A rather unusual article covered methods for handling uncertainty produced from left-censored data and nested sources of error (48). Practical exploratory experimental designs were discussed (49), as were analysis of variance (50) and ordinary regression methods (51). Frank discussed the motivation for and principles of biased methods for regression (52).

Multivariate methods also received considerable attention. Tutorials on analysis with latent variables (53), cluster analysis (54), quantitative structure activity relations (QSAR) (55), target transformation factor analysis (56), and spectral map analysis (57) appeared during the period. Mixture analysis by multivariate methods was discussed in three tutorials (58-60), and new fuzzy methods for calibration and classification were covered by Otto and Bandmeier (61) and by Otto (62). Signal processing methods were the subject of three tutorial articles. Brereton covered the Fourier transform (63), Rutan discussed real-time optimal filtering (64), and Petkov introduced optimization and simulation methods in connection with control (65).

The continuing growth of interest in artificial intelligence (AI) was reflected in a number of tutorial articles. A two-part tutorial (66, 67) covered the features of PROLOG, a language popular for use in expert systems. Gray provided an introduction to the field of artificial intelligence and the DEN-DRAL project, an early effort in AI (68), an article which provoked an exchange of comments with Feigenbaum, one of the pioneers of AI research (69, 70). An expert system was used to aid in design of simulation models for organization of an analytical laboratory in another tutorial article (71).

Applications of chemometrics was the subject of many tutorials during the past 2 years. Several papers appeared on the application of chemometric methods to chromatography (72-77). Three papers discussed chemometric methods in pharmaceutical and clinical chemistry (78-80). Other articles discussed chemometric methods in multidimensional

fluorescence (81), materials analysis (82), and industrial processes (83). Applications of chemometric methods in geochemistry (84) and environmental analytical chemistry (85) also appeared.

Regular tutorial columns are offered in a few journals. *Chemometrics and Intelligent Laboratory Instrumentation* provides one, or sometimes two, tutorials in each issue. The topics and the level of treatment of these tutorial discussions vary widely. Mark and Workman continued their coverage of basic statistics in their column "Statistics in Spectroscopy" in *Spectroscopy*. In addition to introductory-level treatment of such topics as the t-statistic, one- and two-tailed tests and the distribution of means, they have interspersed philosophical discussions on the meaning of statistical testing and biased and unbiased estimators. This column continues to serve a vital educational role for those spectroscopists with an interest—but little background—in the statistical underpinnings of the new chemometric methods that now come on their instruments. Other journals, including *Trends in Analytical Chemistry* and *The Journal of Chemometrics* also offer occasional tutorial articles.

A number of articles using chemometrics methods to teach chemistry were published in the last 2 years. Pattern recognition was used to aid in ion identification schemes (86, 87), and a simulation program was used to illustrate error magnification in multicomponent spectroscopic analysis (88). Teaching of chemometrics in a more formal sense also was the subject of two papers. The structure of a postgraduate course in chemometrics was described in one paper (89), and the use of new software in teaching chemometrics was discussed in the other (37).

STATISTICS

A substantial increase in the number of papers reporting the use of statistical methods occurred over the past 2 years. Many authors included routine statistical procedures along with other work, an encouraging trend. Others published work which is more directed to the development and evaluation of novel statistically oriented methods for analysis of chemical data. A selection of these papers is offered below.

Sampling strategies were among the concerns addressed. Multivariate statistics were used to direct representative sampling of river water (90), and a relative semivariogram aided in optimizing sampling for stream monitoring (91). A seasonal Hodges-Lehmann estimator was coupled with Monte Carlo simulation to design sampling strategies for estimating step trends in water quality (92), and a sequential analysis-directed sampling scheme was used to lower detection limits for particulates (93).

Statistical considerations in estimating detection limits were explored by several authors. Maximum likelihood and minimum χ^2 methods were used with several distributions to estimate detection limits (94). The criteria for detection of analytes were outlined (95), whereas Currie (96) discussed the role of analytical standards in establishing criteria for various decisions required in trace analyses. The effect of the calibration model on detection limit estimates was considered (97), and the meaning of the term "detection limit" was reconsidered in detail (98). New statistical methods were also developed for comparing sets of water quality data with multiple censored values from measurements below detection limits (90), for detecting trends in the presence of multiple censored measurements (100), and for making inferences about the mean from data with multiple censored values (101).

The statistical aspects of interlaboratory comparisons were also of considerable interest. Horwitz (102) offered a protocol for the design and conduct of collaborative studies, and the multivariate statistical evaluation of interlaboratory studies were reported from results of principal component analysis (103), nonlinear mapping, and linear discriminant analysis (104). A criticism of earlier tests in interlaboratory studies was also reported (105). A statistical justification was provided for relating interlaboratory coefficients of variation with concentration (106).

Many authors were concerned, understandably, about the detection of bias in analytical results. A quality assurance program was reported for measuring bias and precision in an analytical laboratory (107). Mark (108) reported a method for determining the true accuracy of an analytical method. The critical assumptions underlying the statistical methods

in ASTM water analysis were discussed (109) and a set of additional statistical tests were proposed. Control of the bias in analytical results was evaluated for single- and multiple-lab assays (110), and detection of systematic error in an analytical method by weighted regression was discussed (111) and verified by simulations. Error in the dependent and independent variables measured in an analysis was considered for estimates of analytical uncertainty in X-ray spectrometry (112) and for evaluation of error in the statistical moments of chromatographic peaks (113). A minimax method was reported for combining means that accounts for bias in those means (114). That approach was criticized (115) and defended (116). Evaluations of reliability of analytical results from bioassay and clinical tests were also reported. A comprehensive set of criteria for measuring the reliability of analytical results was suggested (117). Another paper offered a new measure of reliability which included both the bias and precision (118). Statistical issues were reported for carcinogenicity in animal bioassays (119, 120).

Robust statistical methods continue to see increasing use in analytical chemistry. A robust statistical procedure was used to monitor accuracy and precision of chemical analyses (121), and robust estimation of means and variances was used to evaluate bias in analytical procedures over an extended concentration range (122). Robust L, M, and W estimators were also found advantageous in providing summary statistics in geochemistry (123).

Several novel methods for examining the distribution of chemical data were reported. Identifying the true distribution of data can be troublesome. Quantile-quantile plots have been used to characterize unknown data distributions (124). Elder (125) reported the use of distribution models for trace analysis. He observed that the lognormal distribution seems most suited for trace data, especially as the coefficient of variation increases. The effect of normal standard errors on the lognormal distribution was also studied (126). The variation of analytical precision with concentration was studied for a large number of geochemical analyses, and the often-assumed logarithmic relation was not found (127). Instead a weighted regression indicated a linear relation. Polarographic data collected over a wide sampling range have also been shown to be heteroscedastic, and a weighted least-squares method is suggested for log-plot analysis of polarographic wave shapes (128).

Other statistical papers of note included one on finding the optimum working range in spectrometry by a new approach to the propagation of random errors (129), one on the statistics of pipette calibration, with consideration of serial correlations introduced by evaporation (130), and two papers offering helpful advice on rounding of least-squares parameters (131) and on the proper and improper use of correlation coefficients (132).

OPTIMIZATION

Increasingly, mathematical methods for optimization are used in routine analytical measurements. The number of papers concerned with optimization of instrumental responses has significantly increased. Many of the papers discussed optimization of experimental conditions for chromatographic separation, for automated wavelength selection in multicomponent analysis, and for optimization of the atomization process in atomic absorption spectrometry.

As usual, the sequential optimization based on some form of the simplex algorithm was heavily represented in work published during this period. Those interested in applications of the simplex method will want to refer to the review by Berridge (133), who covered the use of sequential optimization methods in liquid chromatography. Estimation of error parameters from the optimal response of a function was the subject of an exchange of comments (134, 135) on the use of a quadratic approximation method for describing the response in the region of the optimum. Many of the papers using simplex optimization combined it with other mathematical methods. A peak recognition algorithm was coupled to simplex optimization for automated optimization of liquid chromatographic separations (136), while Lagrange functions were used with the simplex to optimize temperature-programmed gas chromatographic separations (137). Including a model for the response function can speed convergence with simplex optimization. This method was used for optimization of flow injection determinations (138) and for solution of

species distributions in complex equilibria (139). When a model is not available, nonlinear interpolation between data can also be used to improve convergence to the optimum (140). Sequential methods other than simplex are sometimes attractive. A Powell conjugate-gradient optimization method was used to optimize a flow injection determination in fewer steps than the more conventional simplex method (141). Optimization of separations by following the path of greatest slope on the response surface also worked well (142).

Simplex optimization methods are known to be prone to difficulties with local optima, a problem that can be avoided with more exhaustive searches. A full, exhaustive search is not efficient, however. Many authors directed effort at improving the efficiency of search methods. Monte Carlo optimization methods were discussed for atomic absorption (143) and wavelengths selection (144). These were shown to be attractive for complex, temporally unstable systems requiring optimization. Selection criteria for minimization of error were reported for wavelength selection by exhaustive search (145) and overlapping resolution mapping and ideal separation criteria were used to aid in the identification of optima in selections of mobile phase compositions in liquid chromatographic separations (146). Optimization of the response using cyclic alternating variable searches, where the grid step size is changed on second and subsequent cycles, was demonstrated and compared to simple optimization for atomic absorption spectrometry (147). Probably the most promising of methods for finding the global optimum does not require an exhaustive search, however. The simulated annealing algorithm, an algorithm that has the ability to "walk" out of local minima that would trap a wandering simplex, is receiving much attention in physics for use in locating global optima. Kalivas has published the first application in analytical chemistry; his group used simulated annealing methods for location of optimal wavelengths for multicomponent analysis (148).

In addition to locating the optimum, it is sometimes also necessary to describe the entire response surface as part of an optimization strategy. A central composite design and nonlinear regression were used to model the response surface for a reversed-phase ion chromatographic separation (149), for determinations of lead by electrothermal atomization and atomic absorption (150), and for stability studies of amphotericin B in aqueous media (151). Fractional designs are often necessary because of the number of experimental variable that may affect the response. These were used to study platforms in atomic absorption (152), and Plackett-Burman fractional designs were used for ruggedness testing in liquid chromatography (153, 154). Juhl and Kalivas evaluated the criteria used in developing experimental designs for selection of optimal wavelengths in multicomponent analysis (155). Modeling of the response surface was demonstrated for non-designed data by partial least-squares regression methods (156) and for two designed data sets by principal components analysis (157). And sometimes the optimal model is "all" that is desired. Osten used a cross-validation approach to decide on the optimal regression model with the PRESS statistic and F-tests (158).

Several novel approaches to optimization of chromatographic separation addressed the generation of response functions from the measured chromatogram. The effects of chromatographic peak tailing were considered (159, 160), and it was shown that an optimization criterion that accounts for tailing effects gave superior separations. Optimization of the resolution of isocratic separations was shown to be possible from a small set of gradient chromatograms (161). Optimization of multisolvent systems for reversed-phase liquid chromatography was also discussed, using a method based on multicriteria decision making (162), and an expert algorithm has been incorporated into the optimization of another chromatographic separation (163). The information content of an overlapped chromatogram was used as a new optimization criterion (164). Although other use of information theory in optimization was rare during the period, Eckschlager (165) continued his work in the area with a paper discussing the effect of heteroscedastic and homoscedastic error on information content in an analytical determination. He pointed out the importance of the analysis of standard reference materials and gave rules for avoiding null information content in analytical results. Although it is not mentioned explicitly, information theory also plays a part in optimizing the data

acquisition during a kinetic experiment (166). In this work, several possible data collection schemes that increase precision are considered.

Finally, two papers considered the optimization process in terms of quality control. Miah and Moore (167) discuss the identification of response functions and performance statistics which are less sensitive to time-dependent fluctuations. They consider the idea of parameter design in chemometrics and they mention its resemblance to the Taguchi method. Adaptive control is used to determine optimal conditions for biomass production in a continuous fermentor, on-line, in the second paper (168). This method uses a dynamic model and a variable-step-size optimization that depends on the quality of the process model, which is identified in real time.

SIGNAL PROCESSING

Recent publications in signal processing are characterized by increasing sophistication in the methods employed to improve the quality of analytical data. Papers on digital filters and maximum entropy methods dominated the work appearing during the past 2 years. Maximum entropy methods, long the subject of considerable debate in the physics journals, are now receiving attention from analytical chemists. These methods are useful for simultaneous signal sharpening and noise reduction. The formalism of maximum entropy processing was reviewed and applied to photon correlation spectroscopy (169) and to hyperfine distributions from Mössbauer spectra (170). Maximum entropy methods can also be used to deconvolute overlapped peaks. A general approach using information theory and maximum entropy was developed for treating deconvolution problems (171). It was also applied to X-ray diffraction data. Levy et al (172, 173) examined deconvolution of 1-D and 2-D nuclear magnetic resonance (NMR) signals and found results that were as good as or better than conventional signal processing based on Fourier transformation and curve fitting. Newman et al. (174) also investigated maximum entropy methods for processing of NMR data, where they were compared with the simpler, faster, minimum-area methods. Another method for enhancing resolution and minimizing noise, the Marple algorithm (175), was tested on submillimeter wave Fourier transform spectra, where less bias in spectral line estimation and less splitting in line shapes were observed than with maximum-entropy methods.

Signal processing with help from the Fourier transform also continues to be popular. Miller discussed some methods in a brief review of the applications of the Fourier transform in chemistry (176). Fourier transform methods for self-deconvolution, done without an explicit convolution operation, were the subject of another report (177). The Fourier deconvolution and maximum entropy methods were compared for decomposing overlapping Raman spectra (178). Advantages and disadvantages of both methods were discussed; the recommended approach combines both methods. Another report compared Fourier self-deconvolution and iterative, nonlinear deconvolution methods for Raman bands (179). The merits of six apodization functions for Fourier self-deconvolution were studied for the analysis of single peaks (180). Apodization functions for more general data analysis in Fourier transform spectroscopy were also examined systematically (181). Two papers considered the interpolation of Fourier transform spectra. One gave interpolation functions for common apodization windows (182). The other considered the effects of noise, time-domain damping, and zero-filling on the resulting line shape (183). Spline functions were used in a Fourier-transform package for deconvolution and differentiation intended for small computers (184). Fourier deconvolution was used for a study of the impulse response functions associated with each part of a flow injection manifold (185). Fourier series-based fitting was used to extract information and to permit automated assay from voltammetric waves (186). The Hadamard transform, often mentioned in conjunction with the Fourier transform, but seldom the subject of much published material, has at last gained the interest of several groups. An introductory review summarizes work with this transform (187). In spectroscopy, the invention of new masking technology has made Hadamard spectrometers feasible. Dyer et al. have carefully examined the effects of nonidealities in Hadamard masks on signals (188), and they have examined methods for fast recovery of spectra encoded

with defective masks (189, 190). The application of Hadamard transforms has spread beyond spectroscopy, too. Hadamard-transform cyclic voltammetry has been reported recently (191). Fourier- and Hadamard-domain spectral representations were evaluated by cluster analysis to determine the reduction in information content with truncation (192).

Reviews of finite impulse response (193) and infinite impulse response (194) filters provided introductory overviews of the many types of digital filters available for signal processing. Adaptive signal processing methods were applied to enhancement of noisy Raman spectra by Jordan and Dyer (195). Savitzky-Golay filtering methods remain popular. New methods were reported for generation of Savitzky-Golay polynomial smoothers for one (196) and two (197) dimensions. Conventional polynomial smoothers were compared with binomial and alternating binomial filters for removal of interferences in ultraviolet spectroscopy (198) and with Wiener filters for smoothing in electron spectroscopy (199). A finite impulse response deconvolution filter was used to resolve overlapping Mössbauer spectra (200). A new algorithm based on the minimum-negativity constraint was reported for restoration of Fourier spectra (201). Digital filtering methods are often demonstrably superior to older, but simpler, methods, but occasionally, exceptions are found: a matched filter was found to provide spectral estimates from Lorentzian spectral features that were inferior in quality to those obtained from repetitive measurements made at a single frequency (202). Several groups explored digital filtering of interferograms. Bjerga and Small filtered interferograms to improve reconstruction of gas chromatograms (203). Brown et al. (204) used the Kalman filter to filter flow injection responses in real time and to filter interferograms from diffuse reflectance spectrometric measurements, while Fellingner, Pap, and Inczedy (205) used the extended Kalman filter to curve-fit exponentially modified Gaussian signals in the frequency domain.

Other interesting methods reported for processing of data included a paper on the use of proportionally spaced cubic B splines for approximation of titration curves and other sigmoidal functions (206). Several methods for the location of peaks and identification of band shapes were also reported. A sliding pivot method was shown as capable of locating peak maxima in spectra as second-derivative methods (207). Its avoidance of derivatives minimizes the noise enhancement effects often seen with derivative methods. A new method for the resolution of spectra using iterative least squares and Fourier transforms (208) was reported. No assumption of line shape was necessary. Another method automatically selects between Gaussian and Lorentzian line shapes in resolving spectra (209). Comparison of standard spectra from a library and experimental spectra are often done with a fast, simple, cross-correlation routine. The sensitivity of the cross-correlation coefficient at zero lag to noise has been reduced by autocorrelating the cross-correlation function. The method is demonstrated on Mössbauer data (210). Cross-correlation was also used to study protein spectra obtained in aqueous solution. A generalized cross-correlation technique was reported (211). Processing of the absorbance-time curves in electrothermal atomization was improved by use of linear sliding means and correlation of the time-varying absorbance. The detection limit and the analytical precision were improved by 2-3-fold (212). Derivative methods remain popular for resolving overlapped responses. A new approach was reported where the deconvolution is performed by expanding the measured function with its derivatives (213). Taking a derivative usually increases the noise in a response, but a paper appeared that suggests a simple, new method for generating derivatives (214). The theoretical basis for the method was presented. Deconvolution and differentiation methods for sharpening signals are compared in another recent paper (215). The general validity of the deconvolution method which uses an excitation profile identical with the light-pulse shape, a common approach to deconvolution of transient signals such as those seen in time-resolved fluorescence, has been questioned (216). A nonlinear deconvolution algorithm was developed for analysis and resolution enhancement of back-scattering and reaction spectra (217) and another was reported for Auger spectroscopy (218). Jansson's algorithm, another nonlinear deconvolution method, was evaluated for deconvolution of poorly resolved gas chromatographic peaks (219)

and near-infrared spectra (220). Yet another nonlinear algorithm, this one a peak-clipping method that takes the statistics of the background into consideration, was reported to improve quantitation in X-ray spectrometry (221). Three papers considered the effects of another type of statistics on signal estimation: the statistics of stochastic processes. One paper used a variance function to characterize the homogeneity of two-phase solids (222). Concentration fluctuations were detected that were not visible in the original data. Two other papers used linear prediction in conjunction with NMR data collection to significantly decrease data collection times for 2-D NMR of complex biomolecules (223, 224).

Relatively little appeared that was specifically concerned with image analysis. However, Geladi and Esbensen considered the utility of image analysis in chemistry (225) and noted the need for multivariate data analysis that results from collection of "images" of all types, conventional and nonconventional. Two-dimension thin-layer chromatograms were examined with image processing methods (226), as were two-dimensional electrophoresis gels (227). Hierarchical image processing methods were employed to analyze arrays of spots on electron diffraction patterns (228).

A limitation of all electronic signal processors is the speed of execution of complex algorithms. Even with highly parallel algorithms, processing takes time. For some time, investigators in electrical engineering have been trying to circumvent this limitation by designing optical signal processors. These inherently parallel processors operate at the speed of light, and they would seem to offer significant advantages over conventional processing. Use of an optical processor introduces other complications, though. High-speed photodetector arrays—a sort of interface between the optical processor and the conventional digital processor world—are an important link in hybrid processing systems. Their capabilities and current limitations for signal processing applications were reviewed (229). Bialkowski and Herrera (230) have tried a simple optical processor, using a matched filter, for real-time analysis of photothermal spectroscopy data. Results from optically processed data did not compare favorably to those obtained from more conventional—but slower—electronic processing.

Finally, it should be noted that, while signal processing has gotten more accessible, it has not necessarily gotten simple. Williams and Salin point out some of the pitfalls awaiting those who blindly estimate detection limits from transient signals (231). They show that some computational methods do not produce valid 99.9% confidence limit estimates and that the deviation depends on how the analytical transient is detected and how the standard deviation of the transient is determined.

FACTOR ANALYSIS

The literature of factor analysis and factor-based methods has been growing dramatically with each review period, and the present one is no exception. The number of papers reporting methods using some sort of principal components decomposition is now very large, and some selection is necessary. The emphasis here will be placed on papers offering insight into improving, not just applying, factor-based methods. A recent review by Gemperline (232) provides a needed update of much of the field of factor analysis. Other reviews by Bracewell (233) on biochemical applications and by Solomon (234) on surface spectroscopy offer good overviews of many applications. Factor analysis is becoming a useful tool of the spectroscopist, either alone or combined with other techniques. The spectra of species present in molybdate solutions over a pH range from 2 to 5 were determined by factor analysis (235), and factor analysis was used with Fourier self-deconvolution methods and nonlinear least-squares fitting to analyze the carbonyl stretch of CD_3COOD in D_2O (236). Factor analysis was compared with least-mean-squares fitting of Auger spectroscopy, where it was found superior in detecting a chemisorbed bonding state (237). And efforts continue to be made to explain chemical effects from suitably rotated eigenvectors. An oblique procrustes transformation was used to rotate factors from gas chromatographic retention data on different mobile phases in an attempt to explain their retention characteristics (238).

Considerable effort has gone into the use of factor methods for analysis of three-dimensional data such as 2-D NMR and

chromatograms. Rank annihilation has always been popular for analysis of three-dimensional, bilinear data, but a new, generalized algorithm may make it more attractive (239). Rank annihilation was also demonstrated on second-order nonbilinear data, first with simulations and then on *J*-coupled 2-D NMR (240). This new rank annihilation method can also be used to perform quantitative analysis in the presence of unknown spectral interfering substances, as Wilson and Kowalski demonstrate (241). On incompletely modeled data, the method outperforms other rank annihilation methods and, not surprisingly, multiple linear regression. Target testing also continues to be popular. Missing data can be estimated by iterative target testing (242), and iterative target testing can be used to track peaks in chromatographic separations, as several authors note. The effectiveness of target testing for peak identification was explored by Strasters et al. (243), who considered the effects of chromatographic resolution, spectral similarity, and relative concentrations on the results, and by Seaton and Fell (244), who used analysis of variance to explore the same effects. Lorber and Kowalski (245) also examined the numerical and statistical properties of target testing and iterative target testing methods in a brief communication. Occasionally, there is no target model available, and other approaches must be explored. Gampp et al. (246) discuss the analysis of data from spectrophotometric titrations with and without an underlying model based on chemical equilibrium. Factor analysis with the pure peak assumption was used to enhance resolution of tandem mass spectra (247), and an iterative key-set method (248) was proposed for extraction of pure spectral responses. Another self-modeling factor method was used to resolve mass spectra from gas chromatography/mass spectrometry (GC/MS) experiments (249). And the Lawton-Sylvestre method for self-modeling curve resolution has reappeared in yet another form, this time to aid in dealing with background effects in flow injection analysis (250).

Determining spectra, with or without suitable target models, is not always simple. A new method which can be an aid where time-dependent data are available, and where species concentrations change over the observed time period, is evolutionary factor analysis (EFA). Maeder and Zilian (251) demonstrate the use of this method for resolving overlapped chromatographic peaks into concentration profiles and absorption spectra. EFA was also used to resolve spectra of stearyl alcohol in CCl_4 (252) and to resolve complex mixtures in flow injection analysis (253). Closely related methods were reported for identification and purity control in liquid chromatography (254, 255) and for identification of organic vapor sources in gas chromatography (256). Factor methods have also been used for depth profiling of materials with secondary ion mass spectroscopy (257) and Auger spectroscopy (258).

Canonical correlation methods, not-so-distant relatives of factor-based methods, also received continued attention. Canonical correlation was used to detect dilution of orange juice (259), and it was combined with factor analysis to aid in the chemical characterization of hydrocarbons from pyrolysis of coal (260). Canonical correlation was also used to aid in one of the most disputed steps in factor analysis: deciding on the true rank of a noisy data set. Tu et al. (261) used the method to analyze the *eigenvectors* from factor analysis and demonstrated the method on fluorescence data. This is certainly a novel approach worthy of additional exploration.

The difficulty of selection of the true rank of the data was underscored by three studies. Malinowski continued in his efforts at identifying the number of significant eigenvalues, this time with a statistical criterion based on an F-test applied to the reduced eigenvalues (262). In another, a new test on eigenvalues was offered (263). This test, based on the variation of the eigenvalues as a function of the number of retained components, was estimated to be 80% successful, with failure coming from improper data selection rather than any weakness in the method. Another study, done to explore the causes of drift in atomic emission spectrometry, pointed out other pitfalls. Correlated multielement effects led to misassignment of variance, which was only detected upon examination of the *eigenvectors* and simulation of the experiment. The authors (264) urged caution in interpreting principal components.

RESOLUTION

The resolution of overlapped responses by some sort of

curve-fitting procedure which uses separate models continues to increase in popularity. This method is to be distinguished from deconvolution, which concerns the removal of instrumentally caused broadening from a response. Deconvolution methods are discussed in the section on signal processing. The vast majority of work aimed at resolution of overlapped responses concerns the use of derivative ultraviolet and visible spectra, with a simple least-squares fit. While the many papers typical of this sort of work are not referenced in this review, for reasons of space, they are covered in another recent review (265). Weyer (206) discussed the use of derivative nodes for resolution of peaks in near-infrared spectrometry in another review. Multivariate techniques for resolving overlapping peaks into components, including some factor-based methods, are also discussed in a review of automated peak recognition in chromatography (267).

A wide range of methods have been tried for resolution. Nonlinear least squares was used to resolve fused NMR peaks, with excellent results (268), and a constrained, iterative method was used on 2-D NMR and 1-D NMR peaks (269). An integer arithmetic algorithm was used to resolve overlapped peaks in γ spectroscopy in real time; the method is claimed to provide mainframe speeds and accuracy on a 16 bit computer (270). Two different resolution algorithms—a simple curve-fitting method and a Bayesian method—were compared for proton-induced X-ray emission spectra (271). The Bayesian method worked better when many overlapping peaks occurred and in regions with poor counting statistics, but it required a large computer to run. Iterative least-squares fitting was used to compare standard reference spectra with a sample infrared spectrum; this approach permitted both qualitative and quantitative analysis (272). Another group used factor analysis and curve fitting to resolve infrared spectra of ketones and ethers in aqueous solution (273). The simulated annealing algorithm was used to resolve complex NMR spectra containing noise (274). Two papers considered the resolution of chromatographic data. In one different distribution functions are used to describe chromatographic peak shapes, and then these shape functions are curve-fitted to several different chromatograms (275). The log-normal distribution was found to best describe peak shapes and to best resolve overlapped profiles. Vandeginste et al. (276) compared chromatographic resolution based on self-modeling curve resolution and on curve fitting of peak profiles in another paper.

Kalman filtering methods also continue to be investigated for resolution of peaks. Several authors were concerned with the information available in the filter innovations sequence. The reliability of filter estimates for a multicomponent analysis was shown to be related to the normalized autocorrelation of the filter innovations (277). The effects of a poorly defined model are also felt in the filter innovations. A peak shift between model and data causes changes in the innovations sequence that can be used to detect the direction and magnitude of the shift (278). Adaptive Kalman filters can correct the filter model for sections of poorly modeled data, based on the filter innovations. Improvements of the simple-optimized adaptive filter were evaluated for several new optimization metrics based on the filter innovations (279). A number of papers appeared concerning the application of Kalman filters to chromatographic systems. Hayashi et al. reported three papers on the use of simplified Kalman filters for resolution of overlapped chromatograms measured with a single-wavelength detector (280–282). They showed that chromatograms resulting from overlapped injections could be handled with a reduced-dimension Kalman filter, whether or not solvent peaks were present in the overlapped chromatograms. Barker and Brown (283, 284) considered the resolution of simultaneously overlapped chromatographic and spectroscopic peaks measured with diode-array spectroscopy. They showed that to adequately describe small spectral changes occurring over the wide range of concentrations in a chromatographic peak, a spectral library model was helpful. A one-dimensional Kalman filter was developed and applied to poorly resolved liquid chromatographic peaks. This was found to work as reliably as a multidimensional filter for peak resolution, but the speed of operation was much higher without matrix operations (285). This one-dimensional filter was applied to a robotic system for total analysis of solid dosage formulations as measured from chromatograms generated from overlapped injections (286, 287). Information theory and

Kalman filtering were combined for evaluation of optimal chromatography, with the "best" chromatogram being defined as that which transmits the maximum amount of mutual information in unit time (288). Information theory was also used with the Kalman filter by Rutan et al. (289) to determine optimal designs for multidimensional fluorescence experiments.

In any method of resolution by curve fitting, the question of model observability must be answered. Highly overlapped models may lead to poorly conditioned regressions, and the accuracy of the concentration estimates can suffer. Kalivas (290) reported a practical statistical procedure which tests for the presence of spectral overlap among the pure-component spectra and simultaneously assesses the degree that concentration estimates may be degraded. Kalivas and Lang (291) also considered the effect of the condition number of the spectral model on the analytical error. They used linear programming to obtain estimates of the lower bounds for the errors.

CALIBRATION

The measurement of analyte concentrations in mixtures of several components is probably the fastest growing area of chemometrics. Many methods for peak resolution can also be used to provide component concentrations, but interest in multicomponent analyses has concentrated over the past 2 years on factor-based methods such as principal components regression (PCR) and partial least-squares regression (PLS). Most of the applications of multivariate analysis continue to be published for spectroscopic measurements, especially those made in the infrared and near-infrared regions, but the use of these methods has widened considerably over the past 2 years. Calibration schemes are now used in potentiometric analysis, for example. A review discusses the calibration methods and instrumentation requirements for arrays of ion-selective electrodes used as sensors (292).

A few papers appeared on traditional methods of calibration, but even these have been influenced by the multivariate philosophy sweeping the field. The venerable standard additions method was modified to use two-response measurements, so that two straight lines result. Their intersection provides the concentration estimate (293). Cross-correlation was used to calibrate spectra obtained from extended X-ray fine structure measurements of binary mixtures (294). Two other papers considered the error in estimation of infrared spectra by cross-correlation analysis of mixture spectra. Simulations were used to determine the behavior of the error (295), which was found to depend on the weighted superposition of component and interferent spectra (296).

The literature published during the past 2 years was dominated by applications of PCR and PLS, as noted above. Two papers compared these calibration methods with calibration based on multiple linear regression for infrared (297) and near-infrared (298) data. Three other papers concerned the multivariate calibration of substances in blood. Lodder et al. (299) assessed the feasibility of determining serum cholesterol and triglycerides by near-infrared reflectance spectrometry and multivariate calibration. PLS calibration was used to determine glucose in whole blood by infrared spectrometry with attenuated total reflection. A cross-validation strategy was used to optimize the PLS model, which permitted direct measurement of levels of analyte in the normal physiological range (300). A similar approach was also used to monitor uric acid, total cholesterol, triglycerides, and total protein in blood plasma (301). PLS calibration with cross-validation of the calibration model was also applied to infrared emission spectroscopy of polymers (302), to the analysis of highly overlapped photoacoustic spectra from three-component aspirin tablets (303), and to the analysis of mixtures of commercial detergent samples by infrared spectrometry with attenuated total reflection (304). Multivariate calibration by singular value decomposition followed by Ho-Kashap algorithm was used for the determination of cationic detergents by tensametry (305). Other applications of factor-based calibration methods included those concerned with the evaluation of acid-base titration curves (306), the determination of mixtures in flow injection and continuous-flow analysis (307), and the determination of mixtures by inductively coupled plasma mass spectrometry (308). A particularly detailed study of multivariate calibration by PLS was done for the spectrophotometric

determination of metals by a colorimetric reaction (309). This study also investigated the limitations of the calibration by using simulations.

Problems with outlier samples, poorly calibrated background, and drift still plague methods for multivariate calibration. Many authors addressed these problems in recent publications. Naes (310) discussed leverage and influence measures for principal component regression, and he discussed distinctions between different types of outlier samples. A method based on an F-test of the factor model to determine its applicability was used to detect outliers in routine analysis of grains by near-infrared spectrometry and PCR calibration (311). The presence of unknown and uncalibrated components in a sample is also a problem. Lodder and Hieftje (312) report a test for ensuring that the sample falls in a multivariate region explained by the calibration. Sometimes, undesirable effects occur during the calibration. For example, undesired responses from water or from particle size effects may be present in near-infrared responses. Devaux et al. (313) demonstrate that the Gram-Schmidt method can be used prior to calibration to remove these undesirable responses. A multiple scatter correction transform was used to improve linearity in near-infrared analysis. Prediction error was decreased by as much as 68% (314). Improvements to calibration when done in the Fourier domain included less sensitivity to particle size, less difficulties with collinearity and faster calibrations, according to McClure and Davies (315), who demonstrated Fourier-domain calibrations for sugars in tobacco. The selection of calibration samples by experimental design (316) and by a preliminary factor analysis (317) for removal of nonrepresentative and redundant samples was also used to improve the quality of multivariate calibrations. Of course, instrumental conditions are ever-changing, and a calibration cannot be considered permanent. Optimal monitoring of a calibration was discussed by Yfantis et al. (318), who gave a scheme for minimizing total analysis costs, and it was introduced in a brief overview by Kateman (319), who considered the need to correct calibration systems for drift in instrumental response and proposed an expert system for recalibrating as necessary. A validation protocol for PCR calibration was also reported (320).

In addition to calibrating on analyte concentrations, increasing use is being made of the factor-based relation of sample properties to responses in calibrations. The molecular weight and density of distillation fractions was estimated from GC/MS data by PLS calibration (321). Multivariate statistical methods, including PLS, were used to aid in the design of new photochromic glasses (322), while PCR calibration was used to evaluate the quality of used lubricating oils from near-infrared measurements (323). Near-infrared measurements, when coupled to PCR, were also used to predict the quality of gasoline (324). Several different calibration methods were compared in Fourier-domain calibration of hydrocarbon mixtures in high-pressure natural gas, and a P-matrix inverse-regression calibration method was used to estimate energy content directly from spectra (325).

The nature of error in multivariate calibration was of special interest. Lorber and Kowalski (326, 327) considered the propagation of error in calibration methods. The detection limits available from calibration methods attracted the attention of two authors. Delaney (328) considered the calculation of multivariate detection limits for selected ion monitoring experiments in GC/MS, using multivariate regression statistics. Feinberg (329) considered confidence intervals obtained from regression methods used to establish the calibration. He showed that the detection limit is not simply calculated from the confidence interval, and he proposed a new criterion, called the minimum allowable concentration.

The theory of calibration methods was the subject of many studies. Hoeskuldsson (330) discussed the theoretical basis of PLS and PCR in considerable detail. Lorber and Kowalski (331) described a modified version of the partial least-squares regression for multivariate calibration. Their new version permits calculation of leverage values for detection of outliers, gives a direct calculation of the prediction error, and takes less computation time than the usual NIPALS algorithm. A new, multiblock PLS2 algorithm was given by Wangen and Kowalski (332). Geladi and Wold (333) report the use of local factor models for multiway calibration methods. They used a rank map of models for finding empty, one-constituent, and

overlapping constituent regions in a spectrum. A new PLS method for analyzing bilinear data was also reported (334). Finally, two remarkable papers by Sanchez and Kowalski (335, 336) appeared on the theory of calibration. These papers provided evidence linking many different methods for calibration by approaching calibration from a tensorial perspective. They showed that the calibration problem is equivalent to finding the contravariant vector corresponding to the analyte being calibrated. The nature of the model built for the subspace spanned by the variance in the calibration was shown to be the only real difference between such methods as principal components regression, ridge regression, and partial least-squares regression.

PARAMETER ESTIMATION

Fitting of experimental data to theory for the purpose of determining adjustable parameters is an area of chemometrics which continues to grow in sophistication and in application. It used to be that simple least-squares or nonlinear least-squares methods were sufficient for most, if not all, of the problems tackled by the analyst. Recent work with new approaches has extracted information from increasingly complex data and occasionally has called into question the results obtained from some simple methods as applied to some common problems.

A number of relatively well-known modeling problems continued to receive attention. Fitting of spectroscopic profiles was explored with least-squares fitting (337) and χ^2 fitting (338) methods. An improved method for fitting of spectra to standards by cross-correlation was demonstrated on very weak spectra of trace species (339). Fitting of titration data is an area that has been extensively studied. A new method based on the use of Padé approximants has been demonstrated for extraction of activity coefficients and dissociation constants, all determined from a single titration curve (340). Often, the exact nature of the model itself is not certain. Monte Carlo studies have been used to aid in estimating parameters from melting of glasses (341) and to estimate concentrations from γ spectra obtained from well logs (342). Alternating linear and nonlinear least-squares regression was used to estimate parameters for line profiles in noisy Raman spectra containing many overlapped lines (343). Beebe and Kowalski (344) used projection pursuit regression, a method which performs both linear and nonlinear regression as it identifies the form of a suitable model, to responses from arrays of ion selective electrodes to measure Na^+ and K^+ at physiological levels. In the estimation of parameters by nonlinear regression, the linearization step produces a system of overdetermined linear equations. Not all of these equations are of equal value in estimating the parameters. Two criteria are offered for selecting the best linearized equations for fitting the data (345). The methods were demonstrated for a potentiometric titration. Alternatives to least-squares estimation have also been examined. Maximum entropy principles were combined with maximum likelihood fitting to estimate parameters from neutron spectra (346). This combination accounts for Poisson statistics and solves the problem of providing prior probabilities for the estimation. Rutan and Carr (347) compared least median of squares fitting, a robust estimation method, with adaptive Kalman filtering. Both methods were more effective in discriminating against outliers than ordinary least-squares or least absolute deviation regression methods. Least-squares and robust regression methods were also compared in calibration problems with non-normally distributed noise (348). Under certain conditions, robust regression offered an advantage over the usual least-squares regression. Bialkowski (349, 350) explored the estimation of parameters in the presence of noise distributed by Poisson and normal distributions using maximum likelihood estimation. Finally, bootstrap and jackknife methods were given for estimation of errors and confidence regions in nonlinear regression (351).

Notable applications of novel methods for parameter estimation were concentrated in chemical kinetics and in estimation of background responses in spectroscopy. Pardue (352) discussed fitting methods in his overview of kinetic methods in analytical chemistry. A more limited review of data reduction for estimation of enzyme kinetics also appeared (353). It is now well established that the nature of data collection strongly affects the quality of the parameters es-

timated from kinetic systems. A theoretical treatment was given for temporal optimization of enzyme-based reaction rate methods for chemical analysis (354), and a discussion appeared on the dependence of the variance of estimated kinetic parameters on the amount of data fitted (355). Modeling of chemical kinetics was examined by several groups. A linearized kinetic model was used to provide initial estimates of kinetic parameters for other modeling methods (356), derivative and integrated models were fitted to first-order inhibition processes by nonlinear least-squares regression (357), and kinetic models were developed and fitted for competing first-order processes (358). Kalman filters were also used to model first-order chemical kinetic reactions measured by infrared spectroscopy (359) and to compensate for run-to-run variations in first-order kinetics measured by fluorescence (360). The filtering of transient systems was also the subject of a brief review (361). Kalman filtering with information theory was used to optimize fitting of second-order kinetic models as well (362). Other methods for optimization of models included steepest descent fitting methods, which were used to model kinetics in thermogravimetric analysis (363). Submatrix analysis was also applied to chemical kinetics, specifically to oscillating chemical reactions where the rate constants were not known (364). Fitting of other processes closely related to chemical kinetic also received considerable attention. Fitting of time-resolved spectra to exponential models was the subject of many papers. Bilinear regression was used to analyze flash photolysis experiments (365), while Russell and Gouterman used factor analysis and nonlinear least-squares methods to extract nonexponential decay parameters from excitation-emission spectroscopic data (366, 367). Weighted linear least-squares and the rapid lifetime determination method were compared for analysis of a single exponential decay (368) and optimum regions for fitting were given. A brief paper examined the convergence of least-squares fitting of a single exponential to kinetic data and showed that a fitting method previously published for this purpose was flawed (369). Decay with several exponential terms was also examined. A reiterative regression was used with a nonlinear least-squares algorithm for fitting multiple time-resolved fluorescence decay signals (370), while another paper discussed the difficulties in using iterated least-squares methods for fitting parallel decay processes (371).

Other work on parameter estimation included a method for simultaneous fitting and deconvolution of Auger spectra (372) and a damped nonlinear least-squares method for fitting of X-ray photoelectron spectra (373). Papers on fitting of electrochemical models to data included a review of modeling by Rusling (374), a paper on fitting of overlapped polarographic waves and estimation of errors (375), and a method for estimating transition times in chronopotentiometry by piecewise linear regression using dummy variables (376). A novel nonlinear regression on orthogonalized variables (377) and nonlinear fitting with several optimization methods (378) were used to obtain kinetic parameters from voltammetric responses.

Several methods for dealing with background in spectroscopic signals were reported during the past 2 years. Background in Fourier-transform infrared (FT-IR) spectra was corrected by fitting with Legendre polynomials (379), and water signals were removed from FT-IR spectra of aqueous proteins by fitting second-order polynomials (380). An FT-IR background made from the second derivative of the sum of a number of component curves was also demonstrated to be an effective alternate to functional modeling of base lines (381). The variable background that occurs in fluorescence detection of thin-layer chromatograms was effectively removed by modeling it by abstract factors from a factor analysis of blank regions on the chromatogram. The abstract factors were included in the Kalman filter so that variable fluorescent background from the chromatographic plate was continuously compensated (382) in the parameter estimation.

Source apportionment is another area of parameter estimation which relies on factor modeling methods. The effects of analytical precision were examined for source apportionment calculations by simulation. With high source collinearity, the chemical mass balances calculated were unpredictable, while with low to medium source collinearity, chemical mass balances were unreliable at high analytical signal-to-noise ratios (383).

Parameter estimation methods were also used for correction of instrumental artifacts and for instrumental control. An objective method for comparison of electrophoresis gels from difference sources was reported (384). The method, based on matching of estimated parameters, does not require use of internal standards. Nonuniform instrumental broadening in size-exclusion chromatograms was corrected by use of a Wiener filter (385). Kalman filtering methods were also applied to gel chromatographic measurements to enable continuous estimation of chain length distribution in a polymerization reactor (386). Recursive state estimators were used to detect the presence of contaminants in bioreactors by analysis of measurements of biomass and production rate (387). Optimization and control of the process were also possible with this estimator. Optimization through modeling was the subject of two rather unusual papers. The Kalman filter was used to model instrumental response surfaces (388), and the similarity between this approach and more traditional methods based on singular value decomposition was discussed. The Kalman filter was also used to predict changes in the objective function of an optimization and of the statistical tests for measurements resulting from deletion of suspect measurements (389).

Occasionally, some very simple problems are reinvestigated with modern methods, and surprising conclusions result. The full width at half-maximum is one parameter often reported for peaks in many areas of analytical chemistry. Five methods for estimating this parameter have been studied on simulated normal distributions containing noise (390). The second-moment method was found the most accurate.

STRUCTURE-PROPERTY RELATIONS

Chemometric methods for the relation of the structure of molecules to their physical and chemical properties are briefly covered in this section. A comprehensive review of the quantitative structure-activity (QSAR) area (391) has covered other more recent efforts. Chemometric methods used in establishing relations between the chemical structure and toxicological action of compounds have also been reviewed (392). Studies done ranged from small efforts focused on the effects of small structural subunits to a truly large-scale example, in which the toxicity of some 20 000 industrial chemicals, pesticides, and drugs was correlated to chemical structure with the help of cluster analysis of 90 molecular parameters. This work produced a set of clusters that could be used to detect potentially harmful compounds from structure alone (393).

Several studies sought relations between chromatographic retention and structure. The relation between gas chromatographic retention and alkylbenzenes (394), the relation of chromatographic capacity factors and structure of antimalarial drugs (395), and the retention of substituted triazines (396) and halobenzenes (397) all were studied. The hydrophobic liquid-liquid partitioning properties of diadamantanyl derivatives was related to liquid and thin-layer chromatographic behavior through correlation to molecular structure (398), and the octanol-phosphate buffer partitioning of dexamethasone carboxamide steroid derivatives was similarly related to chromatographic capacity factors (399). The experimental and theoretical lipophilicity and electronic distribution of substituted benzamides were correlated successfully (400). In this work, HPLC was used to measure lipophilicity, which was calculated with a π function, while NMR measured electronic distributions which were calculated from ab initio theory.

Characterization of structure-property relations with factor-based models was also explored. Factor analysis and target transformation factor analysis were used to model the reversed-phase HPLC retention of 35 benzene derivatives in two solvent systems. The method was used to predict the retention behavior for a wide range of solutes in a ternary solvent system with varying composition (401). Forty-eight amino acids were characterized by principal components analysis of seven thin-layer chromatographic variables and two theoretical variables. The two significant principal components explained 88% of the variance in the data (402). A similar study, done on 16 monosaccharides measured with 13 TLC variables, gave four principal components that explained 98% of the variance (403). Principal components were also used to relate structure to retention and retention to biological activity for 13 benzodiazepines measured on six different chromatographic

systems (404). Partial least-squares regression modeling was used to characterize the principal properties of aromatic substituents (405), the physical properties of hydrocarbon mixtures from NMR data (406), and the chromatographic retention of chiral indoles on triacetylcellulose (407). Several multivariate methods were used to model the relation between the release rate of griseofulvin from solid dispersions with polymers (408). Nilsson et al. (409) used PLS to relate the mutagenic activity of unsaturated dialdehydes, as measured by the Ames test, to theory obtained from molecular mechanics, while least-squares regression was used to relate charge distributions calculated from SCF-MO methods to pharmacological activity for a series of histamine H_2 -receptor antagonists (410). PLS modeling was used to investigate the different assays used in testing carcinogenicity. Only nine of the 35 assays studied appeared relevant to description of carcinogenicity of chemical substances (411). Structure-property relations were also explored by canonical correlation methods (412), which showed that the property factor space correlated closely with mass spectrometric results and the Kovats retention index. The mass spectral variables followed the degree of unsaturation, while the Kovats index, not unexpectedly, tracked with molecular-size-related parameters.

There also continues to be interest in graph theoretical methods for describing molecules. Applications of graph theory to several areas of chemistry were covered in a review by Balasubramanian (413). Two graph theoretic methods were used to model tissue solubility and metabolic rate constants of halogenated methanes (414), and a graph theoretical approach was used to relate molecular path count to simple sums of ^{13}C chemical shifts (415). An algorithm, with computer code, is provided with a discussion of the applications of edge groups of graphs, among which are included the enumeration of isomers of organic compounds (416). The application of two topological models was demonstrated for the relation of spectral characteristics to the structure of benzodiazepine condensates with ethylene oxide in micelles and in solution (417).

PATTERN RECOGNITION

Nowhere is the process of converting data to useful information more striking than with pattern recognition. The methods of pattern recognition were synonymous with chemometrics for many years (and for some, they still are). Surprisingly, this well-established area of chemometrics has been very active over the past 2 years. Along with an enormous number of applications, many new insights have been made which affect the practice of pattern recognition, especially in areas of display, classification, and unsupervised learning.

Display remains an important part of any pattern recognition approach because, as is well known, the human remains the best pattern recognizer. Methods for display of dendograms were briefly reviewed (418) and some display algorithms were given. A new graphical presentation method was suggested by Steigstra et al. (419). This method, called multi-inductive component analysis, is proposed as an alternative for principal components analysis. A discussion of the theory and an application is given. False-color imaging methods used in aeronautical mapping are suggested as a useful approach to interpretation of chemical data (420). A combination of principal components analysis, fuzzy pattern classification, and false-color imaging is recommended.

The use of fuzzy classification and clustering methods continues to grow in popularity. Fuzzy classification was used to identify double-bond position in compounds from mass spectral data (421), to aid in identification of complex chromatograms by directing the search for reference chromatograms (422), and to track peak position in chromatograms where elution order was uncertain (423). Fuzzy set theory was also used for processing of historical laboratory data (424), where different sample types are sorted into a limited number of clusters. Fuzzy clustering was also combined with the multiblock PLS2 algorithm to identify groups of samples for subsequent prediction of the concentration of volatile components in beer (425). Fuzzy sets have also been used for modeling and control. A fuzzy "physiological state" pattern model was used to control a fermentation process, to permit flexible alteration of the control strategy (426). An expert system aided the process.

A number of other new approaches to classification were reported during the past 2 years. A fast, new clustering method was discussed by Zupan and Massart (427), who applied it to classification of olive oils. Classification is based on the assignment of a multivariate data pattern into one of a set of data clusters, often as measured by some sort of distance. Although many different metrics for distance have been tried over the years, the description of the spatial geometry itself had not really been explored. A new classification method, the metric tensor model, is based on similarity measures which use the scalar curvature function of Riemannian space. This new method for pattern classification is applied to the Iris data set (428). The SOLOMON package was extended to correct for missing or censored data and tested against other classification methods on simulated data (429). Four classification methods were compared on three different types of simulated data and also applied to the Iris set and other real data. All of the classification methods were found to perform about equally well, on average (430). Frank and Lanteri (431) also compared classification methods from the standpoints of prediction and complexity of the classification model. They introduced a new model, CART (classification and regression tree), which may have a number of chemical applications in the future. Frank and Friedman (432) discussed the connections between classification and regression, and used the relation to introduce two new classifiers: DASC (discriminant analysis with shrunken covariances) and RDA (regularized discriminant analysis). They demonstrated with simulated and real data that the performance of these new classifiers were superior to that of discriminant analysis and to that of classification based on soft independent modeling of class analogy (SIMCA), particularly for the small sample-high dimension data sets common in chemistry. Derde et al. (433) reported a new nonparametric class modeling method, while Yendle and MacFie reported a new discriminant method for discriminant analysis when the number of variables exceeds the number of samples (434). Thielemans et al. (435) used convex hull boundaries, along with a principal components analysis, to define classes for detection of animal fat adulteration. They showed that the method properly classified samples, though detection of outliers was a problem, and some false positives occurred. The first classification with the aid of a neural network was reported (436). Six alditols were identified from their proton NMR spectra by the trained network. Preprocessing for classification also received attention. The effect of data transformations on *k*-nearest neighbor transformation was reported (437). Chance classification by linear discriminant analysis was also considered (438).

Because of the large number of applications of pattern recognition methods, a comprehensive list cannot be provided here. Instead representative applications will be cited for applications of pattern recognition methods to problems of concern to analytical chemists. Many of these concerned the interpretation of spectral data. A brief overview provided the philosophy of pattern recognition methods for identification of compounds from spectral data (439). The occurrence of subclusters in larger clusters was investigated in cluster analysis of near-infrared spectral data (440). The method permitted detection of a few hundred parts per million of contaminant in a drug capsule. Principal components analysis and factorial discriminant analysis were used to extract discriminant spectral patterns from near-infrared spectra. By this method, free and bound water could be identified in wheat flour (441). A testing method for raw materials using SIMCA classification of near-infrared reflectance spectra was also reported (442). This was used to identify by an F-test acceptable and unacceptable materials for an industrial process. Discriminant methods were used to reduce emission background and enhance small emission signals from H₂O and CO₂ in effluent from smokestacks. Combustion of gas and oil could be distinguished by the method (443). Cluster analysis and correlation analysis were used to determine characteristics of hydroxide bands in vapor-phase infrared spectra. Free and hydrogen-bonded groups were identified for several different alcohols (444). Two-dimensional NMR has also seen increasing use of chemometric methods. Fuzzy clustering methods were used to aid in extraction of information of imaging NMR (445). Classification methods were used to analyze folded 2-D NMR spectra obtained from COSY tech-

niques (446), and principal components analysis and classification were used to separate mixtures of spin systems, regardless of coupling (447).

Applications of pattern recognition methods in chromatography and mass spectroscopy also received a good deal of attention. Reich (448-450) considered the automated recognition of chromatographic peaks in a series of papers. The *k*-nearest neighbor method was used, and several different distance metrics were tested, in the development of a method that was able to recognize peaks with signal-to-noise ratios as small as one. Varmuza (451) discussed several chemometric methods for selective detection of chromatographic peaks in a short review. Gas chromatographic data obtained on persons exposed to PCBs was examined with the SIMCA classifier (452). A quantitative relation between exposure and chromatographic response was established by PLS modeling. Classification of chromatographic data using multidimensional orthogonal polynomials was demonstrated (453). Cluster analysis and principal components analysis were used to classify chromatographic columns. Nine C₁₈ columns were classified into three groups (454). Cluster analysis was also used to classify two-dimensional chromatographic data (455) and, in connection with mapping and other statistical methods, to distinguish pyrochromatograms obtained on samples from cystic fibrosis carriers from normals (456). Pattern recognition methods continued to advance in applications to GC/MS as well. Dunn et al. (457) report preprocessing, variable selection, and classification rules for identification of toxic compounds in GC/MS with the SIMCA classifier. Scott (458) discussed the use of binary encoding and different distance metrics on classification of mass spectra from GC/MS, also with SIMCA classifiers. A brief review discussed classification of trace organic pollutants measured by GC/MS (459). Principal components analysis was used to help classify fungal colonies measured by GC/MS (460), and several bacteria were classified by analysis of their pyrolysis mass spectra (461). Oil identification by chromatographic and mass spectral measurement followed by classification was considered in three studies (462-464). Applications of pyrolysis mass spectroscopy and chemometrics in environmental research were considered in a review (465). Other papers on pyrolysis mass spectroscopy combined with chemometrics ranged from studies of spruce needles affected by acid rain (466), of food profiling (467, 468), and of characterization of bees (469, 470). Laser microprobe mass (LAMMA) spectrometry has also been combined with chemometric classification methods. Two papers considered the need for careful preprocessing of LAMMA data (471) and the use of the LAMMA method for characterization of polymers (472).

The field of chemical sensors continues to edge toward chemometrics. Simple pattern recognition methods are increasingly used to enhance the selectivity of nonspecific sensors, but the sophistication of the chemometrics software continues to lag well behind that of the sensor hardware. Research trends in solid-state sensors were discussed in a recent review (473). In two applications, classification methods were used to discriminate between compounds detected in automated, solid-state, odor sensors (474, 475). Linear discriminant classifiers were used to classify hazardous compounds detected by a surface acoustic wave sensor (476).

LIBRARY SEARCHING

Automated identification of compounds from matching their spectral or other characteristics with those of standards contained in a library continues to be explored, but the number of papers appearing in this area has dropped considerably over the past 2 years. This decline reflects, no doubt, the success that earlier workers has in designing search strategies, and the interest of many instrument manufacturers in getting working search systems for GC/MS and GC/IR systems. The progress in setting up searches has been reviewed by Coates (477), who discussed instrumental and experimental aspects required for successful implementation of search systems.

Most researches are made on the basis of a similarity metric. Zuercher et al. (478) showed that once spectral features are selected and their relative importance has been fixed, the characteristics of the similarity metric are controlled with two independent parameters, one that determines whether a forward or reverse search is conducted and the other whether

a similarity or classification search is conducted.

New developments concerned with library searching included improvements to infrared library searches, the development of search strategies for searches of ultraviolet spectral data, and the exploration of mixed library searches. Forty-one different infrared search systems were evaluated in a study of the performance of automated spectral identification (479). The changes in data base utilization brought about by advances in spectral searching of infrared data bases were discussed by Lowry et al. (480). A Fourier-domain search system was proposed to aid in distinguishing similar spectra in searches of infrared spectra (481). The search system removed dominant spectral features prior to transformation and comparison steps. The effect of sampling and data collection on the success of searches of infrared spectra was also considered (482). Corrections were proposed to minimize the distortions that arose between data collection by transmission, diffuse reflectance, attenuated total reflectance and photoacoustic techniques. A method was reported for correlation of interferograms from separate GC/FT-IR analyses (483). This correlation of standards and samples was used as an alternative to a spectral search, as it was found to be more reliable in low signal-to-noise situations. Searching ultraviolet spectra is much more difficult than searching infrared spectra, because the spectral information is less easily extracted, and there is usually less information to start with. A Fourier-domain search was used to concentrate information from ultraviolet spectra (484). The effects of noise, frequency-domain peak shifts and background fluctuations were studied in the searches. An alternative approach, based on searches on integrated subsets of ultraviolet data, was also reported (485, 486). This work considered three different methods for identification, including analysis of difference spectra and rank analysis, in addition to the usual dot product method. A search method for automated spectral characterization of 2-D double-quantum coherence ^{13}C NMR spectra was also reported (487). This approach first assigns chemical shifts and then considers coupling information in developing structures. The algorithm is discussed and then applied to the structural elucidation of some terpenoids.

Searching combined libraries is one way to enhance the specificity of a data base, especially when spectral data contain relatively little information. A combined search of chromatographic retention and ultraviolet spectral data, collected by HPLC with diode array detection, was used as a means of identification of 74 organophosphorus compounds. A success rate of 95% was claimed (488). Two-dimensional searching of infrared and gas chromatographic databases, collected in GC/FT-IR analysis, was also reported (489), as was a combined search of infrared and mass spectral databases in analysis by linked GC/FT-IR/MS (490). A 30-component mixture was analyzed to demonstrate the use of the linked analysis system in studies of complex mixtures.

Usually, searches assist in the qualitative analysis of mixtures, but it is also possible to use search methods for quantitative analysis, as Davies et al. have demonstrated (491). They used a data base of infrared spectra, stored as interferograms, and stored with each entry the associated chemical analysis. The unknown is compared to the library, and a small subset of entries is identified, from which the unknown is quantitated. The method was applied to the analysis of nicotine in tobacco.

ARTIFICIAL INTELLIGENCE

The application of artificial intelligence (AI) to problems in chemistry continues to increase. While interest remains high in the development of expert systems for automated solution of analytical problems, research has explained into several new areas during the past 2 years. This area continues to be one of the fastest growing in the chemometrics field. The intense activity in artificial intelligence has prompted several substantial reviews. Gray (492) has reviewed the techniques and tools of AI. He points out that AI is commonly applied in two situations: problems where it is necessary to encode chemical expertise and problems where chemistry is merely an additional domain to which standard AI techniques can be applied. Another review concentrated on knowledge-based systems for interpretation of analytical results (493). The overview by Frazier (494) considered the capabilities and the weaknesses of knowledge-based systems. The difficulties of

handling large amounts of complex data are discussed in a review by Zupan (495). He presented a model for an expert system based on the hierarchical organization of a large amount of data. Recent developments in the hardware and software of expert systems are the subject of two other reviews, one directed at an overview of applications (496) and the other at strategies for the development of limited-domain expert systems on microcomputers (497).

In creating rule-based expert systems, the decisions made cannot be any better than the database used. A test knowledge base was reported for HPLC of pharmaceuticals, so that the knowledge representation features needed to describe chemical knowledge could be examined (498). No single representation method seemed optimal. A pattern recognition method was used to generate rules for the elucidation of spectral features from MS and MS/MS data. The initial work on this project defined inclusion rules, established by correlation of mass spectral peaks with structural elements (499). More recent work has extended automated rule generation to exclusion rules (500). Settle et al. (501) reported on the analytical descriptors required for a combined expert system and information database on microwave dissolution. Knowledge-based peak purity evaluation was discussed for liquid chromatographic responses. A number of simple numerical tests are evaluated by an expert system in deciding whether or not a peak consists of coeluting components (502). The problem of coding structures for the prediction of ^{13}C NMR data, especially for conformations and double bonds, was also discussed, and a new coding scheme suggested (503).

AI methods continue to be applied to problems of structure elucidation. Protein conformational analysis was determined by the expert system PROTEAN, using NMR data. An overview of PROTEAN discussed methods for reducing computational burden (504). Determining protein conformations in solution was also the subject of a study where AI methods of heuristic control were used to decide systematic assembly of structural information, with the goal of excluding the most conformations (505). Molecular modeling of protein structure was directed by AI methods using FT-IR data to aid structural assignments (506). The theory of bond, electron, and reaction matrices was proposed as the basis of a new generation of logic-oriented programs for solution of organic reaction networks and other chemical problems (507).

Application of expert systems to problems in liquid chromatography continues to increase rapidly. A brief review discussed the design of expert systems in liquid chromatography (508), while the expert systems used in HPLC method development funded by the ESPRIT project 1570 were described in another overview (509). The use of AI methods in integrated intelligent instrumentation for chromatography were discussed by Liebman et al. (510). Chromatographic retention-structure relations have been coupled to an expert system for prediction of chromatographic resolution and for suggestion of optimal mobile-phase composition (511). The chromatographic database is based on the alkyl aryl ketone scale. An expert system has been reported for the selection of criteria for optimization of chromatographic separations (512). Other expert systems for optimal selection of columns in isocratic separations (513) and optimization of eluent (514, 515) have also been reported. Even experimental design methodology has been integrated into an expert system framework. Yuzhu et al. (516) report an expert system for ion-pair liquid chromatography, with an optimization module based on a simple 2×2 factorial design and an overlapping resolution map.

Coupling of expert systems with robotics is another area of active research in artificial intelligence. Isenhour and Marshall reviewed progress in the area (517). An expert system was developed to test combined AI-robotics tasks, so that execution times could be minimized and resources optimized (518). Another AI-driven robotic system was used to perform compleximetric analysis (519). This expert system was able to learn from past experience, and it used heuristic rules to make decisions.

Other applications of expert systems included one based on the AI language OP5 for automated interpretation of large electron probe microanalysis data sets (520, 521), a FORTH-based expert system for assisting new users of X-ray spectrometry equipment (522), and an expert system for computer-aided fault diagnosis in vacuum systems for mass

spectrometers (523). Progress toward a steroid-profiling expert system was discussed (524), and an expert system for interpretation of results from screening tests on patients suffering from electrolyte and acid/base disorders (525) was described in two biomedical applications of interest to researchers in chemometrics.

Given the large number of studies in applying expert systems to problems in analytical chemistry, it is inevitable that interest is increasing in design of expert systems to perform chemometrics. Initial work has concentrated on using the logic imbedded in the expert system as an alternative to more traditional chemometrics methods. Expert systems are now being used to interpret infrared spectra of mixtures through use of peak identification and spectral similarity modules (526). A rule-building expert system has been developed to classify mass spectra (527). This classification scheme was better able to classify complex samples, such as bacteria and polymers, than traditional chemometric methods based on linear discriminant analysis. Scott (528) reported on an expert system for classifying GC/MS that outperformed the SIMCA classifier. The SPECTRE expert system, a package for selecting appropriate methods for data analysis, was discussed (529, 530). Expert systems for applications in the analytical laboratory, including selection of chemometric methods, were the subject of an introductory overview (531). Those in chemometrics who fear being replaced by an expert system can take heart from a study by Buydens et al. (532), however. They found that, using two rule-building expert systems on simulated data, certain data structures (not surprisingly, data with correlated measurements or data with outliers) could not be handled optimally by an expert system in classification studies. While it could be detected in some cases that the rules created for classification by the expert system were not robust, this required expertise beyond that available in the expert system. They concluded that the expert systems do not yet possess enough expertise to be used without problems by nonexperts in automated, intelligent instrumentation.

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X-ray Spectrometry

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A. OVERVIEW

This review covers most of the fundamental papers that appeared in the period 1988-1989 in the field of X-ray spectrometry (XRS). Of course, as usual, we have been selective in the contributions included but have tried to be sufficiently general so that both new readers and experts might find relevant literature and necessary details on the recent advances and directions in XRS. All references will refer to English-language articles, unless stated otherwise, although

in a search through *Analytical Abstracts* covering 1988, we found that not less than 14% and 12% of the XRS literature is published in Russian and Chinese, respectively. We have applied a traditional subdivision of the whole XRS field, although we are aware that many papers could be appropriate to more than one section.

In the period under review, several relevant books were published. Two of them are devoted to X-ray fluorescence, XRF (A1, A2). General aspects, current developments, and