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FINAL REPORT

Studies of the Analyte-Carrier Interface in Flow Injection Analysis

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The following report summarizes work accomplished on this project over the past 4.5 years. Work began on this phase of the project on 1 June 1987, and continues in some areas, but support terminated on 31 January, 1992.

Summary of Project and Statement of Goals

The chemical analysis of species in flowing solution has become popular because it provides a low-cost, rapid way to automate many classical methods. The manner in which an injected analyte bolus mixes with the carrier can be controlled, permitting study of well-defined, reproducible reaction zones at the interface of analyte and carrier reagent solutions. Most of the classical methods used to detect the products of the reaction between analytes and reagents in the carrier are not specific enough to permit direct multicomponent analysis of even relatively simple mixtures, however. Two possible routes to enhancing the specificity of the detector are available: (1) enhance the specificity of detection through a competitive reaction of analytes with a species in the carrier, thereby using the dispersion and diffusion properties of flowing systems to effect a distribution of detectable species across the injected bolus, or (2) use a rapidly scanned detector in concert with mathematical methods for enhancing spectral selectivity. The first method is a competitive kinetic analysis carried out in a flowing medium, with a dispersion-controlled mixing of reactants. The second is a direct multicomponent analysis, applied to a transient sample. The two approaches share some common features, since kinetic and dispersion effects complicate the multicomponent analysis, and because rapid spectral measurement is necessary to map the distribution of reactants and products which is required to evaluate the kinetics of a dispersion-controlled, competitive chemical reaction.

This project has as goals the study of rapid multicomponent analysis of transient species in flowing media, the investigation of chemical reactions at interfaces, and the investigation of the effects of competition on the distribution of products from an interfacial reaction. Work required to meet these goals includes development of new methods for rapid multicomponent analysis, and the examination of newer methods of detection for interfacial and transient species.

Summary of Work Accomplished on Project

1. Analysis of Multicomponent Responses in Flowing Systems

To study chemical kinetics associated with a moving, interdiffusing reaction zone, there is a need for spatial analysis of a transient response. This spatial analysis must be coupled with multicomponent analysis, so that mixtures of species with overlapping spectral (or other) responses can be separated quickly. During the past three years, we have investigated spectral methods for rapid multicomponent analysis of transient, overlapped responses, such as those produced by components from flow reactions and by partially resolved components from a liquid chromatographic separation. These methods make use of fast digital filters for the analysis of the rapid-scan spectra obtained from Fourier-transform infrared and diode-array ultraviolet-visible detectors. With this combination of fast data collection and fast data reduction, real-time analysis of mixtures, even mixtures undergoing change through some chemical reaction, as, for example in a flow reaction carried out in a flow injection manifold is now possible. An extension of this work demonstrated the real-time filtering of infrared spectra of atmospheric pollutants taken from moving helicopters and trucks. A novel factor-model of the atmospheric background was used to permit monitoring of target species.

A. Construction of Spectroscopic Detectors for Flow Manifolds:

To test new digital filters, a flow injection system was set up with diode array spectrometer as the detector. Flow cells of 80 μl and, later, 6 μl were used, and care was taken to maintain good flow geometry, so that laminar flow could be maintained. The initial system used a first-generation HP 8451A detector interfaced to an IBM-PC, but this was replaced with a faster HP 8452 detector and 10 MHz IBM-AT compatible computer to increase data transfer rates, which were found to limit the rate of data acquisition, and ultimately to limit data analysis as well. With an IEEE 488 interface, data transfer was efficient enough to permit collection of 30-50 spectra over a 10 second-long flow injection bolus, depending on the spectral range covered. While this rate of transfer is adequate for many tasks, including monitoring of liquid chromatographic separations, it limits the study of the interfacial zones in flow injection reactions, since relatively few spectra can be collected over these regions. Smaller spectral ranges permitted fewer data transfers, which significantly increased the data collection rates. Later work coupled the data collection and transfer to simple digital filtering software based on the Kalman filter (1), so that real-time filtering was possible on the transient responses produced from the flow-injection system. For this simple filter, data analysis times were near 0.5 to 1 second for a diode array spectrum consisting of 100-200 measurements. To increase the speed of data analysis, a digital signal processor (an AT&T DSP-32B) was added to the microcomputer controlling the spectrometer. Studies of the Kalman filter algorithm, executed on the DSP, show that significant time savings are possible. A single step of the Kalman algorithm for a five-state model required 65 μs on the DSP. Further improvements in speed are possible with more sophisticated interfacing of array detector and spectrometer, and by the use of a faster processor and bus, since the main limitation remains data transfer from spectrometer to computer and from computer to and from the DSP accessory. Even without change in equipment used for data collection, other time savings are possible. A study of filtering over limited ranges, where the data contain the maximum information, showed that significant time savings were possible with very little degradation of accuracy or precision.

Filtering of a 20 point spectral subset produced results that differed little from the filtering of a full 250 point spectrum. This work is also being prepared for publication. An overview of the advantages of Kalman filtering appeared in *Trends in Analytical Chemistry*.

A similar flow detection system was set up with a Digilab Model 40 Fourier transform infrared spectrometer, interfaced to an 8 MHz 68000-based data station. The detector cell used for these studies was a Spectra-Tech attenuated total reflectance micro-flow cell with ZnSe internal reflection element. Here, data transfer from spectrometer to disk was very slow, mainly because of the software supplied by the manufacturer, so that real-time tracking of flow injection profiles could only be accomplished by using the commercial "GC" package provided by the manufacturer. This package permitted collection of up to 1 interferogram per second over an extended period, as required for monitoring of flow systems, but data were automatically co-added in this software, so that flow spectra could only be accessed in a partially integrated form. The proprietary nature of the software prevented our making changes to the spectrometer data transfer. While new instrumentation is available to deal with this problem, the design flaws of our Digilab spectrometer prevented collection of useful, real-time infrared spectra, and this effort was abandoned.

B. Studies of Transient Responses in Flow Injection Systems:

To track the distribution of species in a multicomponent flow experiment, a "three-dimensional" Kalman filter (1,2) was used. Initial work was done on simple acid-base reactions in flow injection analysis because these reactions are fast and complete. Previous attempts to study acid-base reactions in flow-injection analysis used species with well-resolved spectra, such as acid-base indicators; in these studies, the only real issues to be addressed in quantitating species are the need for data collection which is rapid enough to define the bolus and the need for measurement of background, so that the baseline can be well-established. We selected reactions where reactant and product had very similar spectra. In these systems, visual identification of the reaction zone - as was done by earlier workers - is difficult. One such system, the nicotinic acid-nicotinate reaction, is shown in Figure 1, along with the filter-derived profile of acid and base species. Integration of the species profile produced areas which were linearly related to the amount injected. Study of this system demonstrated that species' distributions could be followed across a bolus, even when the spectral responses were very similar. Related work involved the competition of nicotinic and isonicotinic acids for hydroxide at the bolus-carrier interface. These acids have similar spectra and similar pK_a values (4.76 vs. 4.96), so that the competition should be high. Not surprisingly, similar profiles were produced for both acid-base reactions at the interface of bolus with the hydroxide carrier.

In this and in other studies, however, a difficulty was noted in the data analysis of species very near the interface: fitting of spectra in this region tended to be less successful, especially when the multicomponent model contained several species with similar spectral responses. This error in data analysis was studied two ways. First, the similarity of component spectra was studied by calculation of the calibration condition number: high condition numbers indicate high similarity in spectra, and near-linear dependence in the filter model, while low condition numbers (near 1) indicate linear independence of spectral components of the model (3). We observed small to moderate condition numbers (2 to 10), and noted that model error was dominant for the models with larger condition numbers. Apparently, the pointwise operation of the Kalman filter has the effect of increasing the apparent condition number, making results from models containing spectrally similar species less reliable when the modeled species are present in roughly equal amounts. Using a vector-based filter algorithm decreased the error. Depending on the size of the filter model (number of components to be quantitated and number of wavelengths to be used in the quantitation), a vector filter can be significantly faster than the alternative scalar filter as well. The second study of model error showed that selection of suitable wavelength ranges

(rather than just using the full range) could be used to minimize the condition number for the calibration model. This reduction has as a side benefit the enhancement of data transfer rates: since less data are transferred and less are subjected to the digital filter algorithm, an improvement in real-time performance results. One advantage of condition number optimization is improved sampling of transient signals. For fixed error in sampling a transient response, alternatively, condition number optimization permitted a decrease in residence time of the bolus in the detector, which allows use of much higher flow rates. These improvements have led to improvements of up to 100% in real-time throughput over our earlier work. One additional benefit from these studies should result: better mapping of the interfacial region. We have already shown, as part of the examination of model error, that manual injection contributes 10 parts per thousand to the total estimation error, mainly through jitter in the bolus width. This jitter is less than that observed from methods based on quantitation from flow peak shape alone, but the jitter makes any attempt to predefine the location of the narrow interfacial region difficult. Fortunately, the improved mapping of the bolus achieved in these studies permits tracking of the bolus-carrier interface over a series of injections.

Modeling the interfacial region was also attempted as part of these studies. Initial studies of flow dispersion-controlled reactions using the work of Painton and Mottola (4) showed that their equations were not an accurate representation of the interfacial reaction. As noted by Hungerford (5), the interfacial reaction seems not to fall into either a simple, pseudo-first-order or second-order regime, as is assumed in Painton's equations. A simulation of the flow and kinetics, along the lines of that done by Bettridge and Wade (6), was tried, but found too time-consuming for a realistic number of reacting molecules. Another approach involves solving the coupled dispersion and kinetics by moment methods commonly used in chromatography (7). However, only moments are available from the analysis. We were able to significantly improve our digital simulation of kinetic effects occurring at interfaces. New digital simulation routines were developed and tested for simple interfaces, such as planar electrodes. These simulations improved the existing "hopscotch" and expanding grid methods first published in the chemical literature by Feldberg and others (8). A study of the short- and long-time error of digital simulations at electrified interfaces is being prepared for submission. This work was extended, and the responses to novel electrochemical excitation sequences we also modeled: in this work, we have shown that a single, general digital simulation can be used to model the interfacial response to *any* electrochemical excitation waveform. Figure 2 demonstrates fits of the general digital simulation to square-wave (Fig. 2A) and a pseudo-random input (Fig. 2B) voltammetric responses. Figure 3 shows the quality of the simulated responses. Comparisons of the simulation versus the responses predicted from Cottrell law (Fig. 3A), and the simulation versus the tabulated values of Nicholson and Shain (Figure 3B) are shown.

C. Development of Kinetic Filters:

A filtering method was developed for second-order chemical kinetics, in order to determine the amount of computational effort that would be required to solve a coupled flow-kinetic problem. A nonlinear Kalman filter was used to filter simulated and real data from second-order chemical reactions. This filter was found to be very sensitive to the use of a proper model for the kinetics present in the data. It also was necessary, because of the degree of model nonlinearity, to iterate on the data. For this reason, several novel ways of analysis of the kinetic data were studied, in order to reduce the computational burden and to decrease the number of iterations required for convergence. It was found that a filtering scheme where selected absorbance data were filtered first in time, then in wavelength, converged fastest. This scheme precludes a real-time coupling of a kinetic filter to the multicomponent analysis, since it requires all of the kinetic data prior to beginning the data analysis. The second-order filter is useful, however, in discriminating between first-,

pseudo-first- and second-order kinetics, a feature that makes it a useful diagnostic tool. The second-order filtering was the subject of a paper published in the *Journal of Chemometrics*.

An additional filtering method was developed and tested for infrared data collected over the course of a chemical reaction. The pseudo-first-order hydrolysis of haloacetic esters in mixed acetone-water solvents was studied. This reaction was convenient because of the size of the rate constant, the variation of rate with the solvent, and because the reaction could be made second-order, if desired, by relatively small changes in the reaction conditions. It was found that the infrared spectral data collected over this hydrolysis reaction were well fitted by the kinetic filter model, but that care was necessary because of the large amounts of spectral interaction between the products of the hydrolysis (haloacetic acids and ethanol) and between the products, solvent and the reactants. The spectral changes that resulted from the interaction of reactants and products made fitting a second order model to similar hydrolysis data unattractive. This work was published in *Analytica Chimica Acta*. Efforts to deal with interactions of this type led to the work on adaptive filtering of infrared responses and to the spectral library calibration work discussed in the following sections.

Finally, a study was made of the utility of fuzzy modeling for distinguishing the chemical kinetic model for chemical reactions whose order and model change as conditions change. For example, the fuzzy modeling is intended to provide a graceful transition from pseudo-first-order kinetics to second-order kinetics. Early efforts with other fuzzy models were promising, and it was hoped that this would offer another way of treating the change of kinetics that occur at the bolus-carrier interface. Fuzzy modeling "blends" models in regions between those where a single model clearly dominates. Results from each model are combined to make fuzzy predictions which might offer improvements over single-model approaches. The fuzzy modeling requires extended Kalman filtering to optimize the model mixture, and it is a natural extension of our earlier efforts to model first- and second-order reaction kinetics with Kalman filters. Fuzzy filtering require an additional optimization step - to identify the limits of the membership functions needed to define the regions of applicability of the fuzzy models - and the calculations needed are extensive. However, it may have uses when the kinetic models change over a region, the case studies in this work. A paper is now in preparation concerning fuzzy Kalman filtering and fuzzy kinetic models.

D. Analysis of Partially-Resolved Liquid Chromatographic Responses:

A flow injection experiment involving multiple analytes in the injected bolus can be taken as a completely unresolved chromatographic response. To test the three-dimensional filtering of flow injection responses, the three-dimensional Kalman filter was applied to some partially-resolved high-pressure liquid chromatographic (HPLC) data. Three studies were performed. In the first, a Kalman filter was used to identify peaks in a chromatogram obtained from infrared spectra measured on output from a reverse-phase chromatographic separation of six species (acetone, methyl benzoate, methyl salicylate, benzaldehyde, nitrobenzene, and ethyl acetate). Despite the similarity of the infrared spectra, identification of each species was simple, even though some chromatographic peaks shifted in location during the time between calibration with standards and measurement of the unknowns. Component quantitation was fairly good, although fairly large detection limits were obtained because of the relative insensitivity of the infrared detector and because of difficulties in the commercial software used in the data collection and storage. Results from the filtering were, in general, superior in accuracy and precision to those generated by more conventional chromatographic quantitation methods applied to the same data. This work was reported in *Analytical Letters*.

Two other studies concerned enhancement of the separation of dopamine and tyrosine. These compounds are reported to be poorly resolved in some reverse-phase HPLC separations (9), and they have very similar ultraviolet spectra. Many of the more

traditional methods for detecting impure chromatographic peaks do not work well with these two species. The first of these studies demonstrated the successful mathematical resolution of highly overlapped tyrosine and dopamine chromatographic peaks. It also demonstrated the need to account for small amounts of detector drift through inclusion of a "drift component" in the filter multicomponent model for the data. This work was reported in the *Journal of Chromatography*.

In this chromatographic study, the model error first noticed in fitting of flow injection data near the bolus-carrier interface also occurred. When the two tyrosine and dopamine amounts were nearly equal, errors in fitting resulted, even with a drift component added. This error was studied in detail, and it was eventually traced to small spectral changes that occur with concentration. In effect, the empirical spectral models measured at one concentration do not accurately reflect spectral data collected over another concentration. The sizable dynamic range of the data over a liquid chromatographic peak (and over a flow injection peak) produces this type of model error. To correct for error in modeling spectra measured at widely varying concentrations, such as those taken under a chromatographic peak, libraries of model spectra were used to describe the spectral model. The built-in predictive mode of the three-dimensional Kalman filter was used to select the most likely library member for the model. This feature permitted the model membership to change as the analyte concentration changed. Not only does this method extend the dynamic range of a calibration, because weakly nonlinear calibrations are also usable as a result of the piecewise linear calibration curve defined by the use of the calibration library, it also permits the modeling of concentration-dependent interactions of analytes, or of analytes and mobile phase components. This study, published in *Analytica Chimica Acta*, led to a great improvement in analysis of flow systems, since much of the model-data mismatch was the result of fitting a single calibration model taken in static experiments to flow data.

2. New Methods for Compensation of Systematic Error in Multicomponent Analysis

One factor which limits routine use of multicomponent analysis is the inability of calibration-based empirical modeling to adequately predict the composition of samples taken well after the calibration step. Often, the poor prediction results from gross error, as occurs when one or more components occur in the sample that were not part of the calibration scheme. Even if all components are calibrated, error may arise from drift in detector response over time. Drift-related error can be difficult to detect with the usual diagnostic tools. Because multicomponent analysis is a critical part of the studies conducted here, the effect of gross model error and drift were studied, with an emphasis on finding methods for correction of these systematic errors in the multicomponent analysis.

A. Compensation for Gross Error in Calibration Models

Gross error in a calibration model can arise from several sources, including omission of species that are present in the sample, omission of interaction of analytes with other analytes, or omission of interaction of analytes with "silent" species, such as the solvent or other species which give no signal at the detector. In each case, the omission leads to the fitting of an incomplete spectral model to the sample data; poor fits often result, and the concentration estimates obtained from these fits may be (and usually are) inaccurate.

Several studies were undertaken to develop filters that could detect gross model error, and possibly compensate for such errors in the model during a multicomponent analysis. The first study continued work begun earlier. All of the studies took advantage of the information contained in the innovations sequence, one of the features distinctive to the

Kalman filter. The filter innovations $v(k)$ are defined as the difference between the predicted measurement and the experimentally observed measurement, namely

$$v(k) = z(k) - H^T(k) X(k|k-1) \quad (1)$$

where $X(k|k-1)$ is the predicted filter state at point k , $H(k)$ is the filter model at point k , and $z(k)$ is the measurement at point k . In these studies, an adaptive Kalman filter based on matching the experimentally-observed covariance of the filter innovations with the theoretical innovations covariance was investigated on various types of spectral data. An earlier adaptive filter was demonstrated to be non-optimal, requiring external optimization by the simplex method (10). This optimization was based on finding the minimum of the logarithm of the trace of the filter state covariance; often, the optimization was quite slow, and 10-15 minutes might be needed for convergence. Because the state covariance of an adaptive filter is not a particularly sensitive measure of state optimality, other optimization metrics were sought in hopes of improving the performance of the simplex-optimized adaptive filter. The filter innovations are a sensitive indicator of state quality and of filter performance, a fact which suggested use of the innovations of the adaptive filter in the search for suitable optimization functions. Several possible metrics were developed and tested on simulated and real data. These included optimization metrics based on the area of the innovations sequence and on the information entropy of the innovations sequence. The information entropy S is defined as

$$S = - \sum_{i=1}^N p_i \ln(p_i) \quad (2)$$

and where p_i is the normalized second derivative (of the optimization metric) at wavelength channel i . In addition to these two optimization metrics, other metrics based on the addition of a penalty function for negative innovations were also developed for the area and entropy functions. Negative innovations result from overestimation of one or more components of the filter model; this overestimation of one component is generally accompanied by underestimation of another component, so that the presence of significant negative innovations is an indicator of filter inadequacy. The last two metrics permitted an adjustable penalty to be applied if innovation sequences producing minimum area or entropy happened to have three or more sequential negative innovations. In this way, noise-related negative innovations did not cause penalties, while negative innovations caused by underestimation would result in a penalty designed to prevent use of these filter results as the optimum. All four metrics cause substantial changes in the nature of the response surface to be optimized. The trace often gave a relatively flat response surface with a sharply defined minimum. The flatness of the surface made searching difficult. For the same filter applied to the same spectral data, using the same two-component model, these new metrics give gently sloping response surfaces with slightly more broadly-defined minima than that obtained with the trace metric. The comparison is shown in Figure 4. A detailed evaluation of all four new metrics against the trace metric showed that the new metrics perform better than the older trace metric, but the dramatic improvement in the speed of optimization is not available from use of these metrics. The area metric with penalty produced, on average, slightly more accurate results than the others, at least for the ultraviolet-visible data sets used to test the filtering. This work was reported in *Analytica Chimica Acta*.

The need for a real-time or near-real-time method for compensation of gross model errors remained, and efforts were made to find an alternative adaptive filter. Early in the project, a new adaptive filter based on correlation of filter innovations was tested, but found to converge slowly. It was nevertheless of interest because it offered a simple, fast way to estimate noise variances for the system dynamics and the measurement processes. With these estimates, other routes to designing adaptive filters are available. Later, a new adaptive filter based on the variance of the innovations process was developed. In this filter, measurements are filtered if the innovation produced from a measurement falls inside a critical window; if the measurement produces an unusually large innovation (which falls

outside the critical window), that measurement is ignored. This method permits a fast, almost optimal filtering of data with an incomplete filter model. The new adaptive filter has been tested on simulated data and on data taken from ultraviolet and visible spectroscopy. It does not require external optimization, and it converges in less than three iterations. It is also computationally simple, so that real-time use is possible. For gross model error caused by omission of a spectrally-responsive component of the sample, this filter was found to produce far better estimates than the simplex-adapted Kalman filter, partial least squares prediction, or other calibration-prediction methods. For gross model error caused by spectral shifts, however, the simplex-adapted filter with area-based optimization performed slightly better, no doubt because of the averaging step built into the covariance matching. This filter produced slightly better results from infrared spectra taken on mixtures of polar compounds. In these mixtures, spectral shifts occurred as a result of analyte-analyte interactions. Papers on the novel adaptive filter, and on its use in calibrations in infrared spectrometry have been submitted to *Analytica Chimica Acta*. Another paper reporting on the use of adaptive filtering in multicomponent analysis has been published in *Chemometrics and Intelligent Laboratory Systems*.

B. Compensation for Drift in Measured Multicomponent Data:

The effects of drift on multicomponent determinations were also examined briefly, again using variants of Kalman filters. Linear drift, one type of drift believed to occur over time in many spectroscopic systems, was corrected with a linear Kalman filter which included drift parameters as part of the filter state. Multiple measurements were required to insure filter observability, since the fitting of drift parameters complicates the filter model somewhat. Filter speed is also decreased slightly by the need to use a more complex filter model. Proportional drift was also considered. Proportional drift is nonlinear, and a nonlinear filter (in the systems dynamics model) is required to extract effects of proportional drift. An extended Kalman filter was used with a multicomponent model to correct for significant proportional drift in data. This filter was computationally efficient, and filter observability was not a problem. Some results of drift correction by Kalman filters are shown in Figure 5, where correction of linear and proportional drift is demonstrated by comparison with a fitting method which ignores the drift. This work appeared in *Chemometrics and Intelligent Laboratory Systems*.

3. Real-Time Data Analysis in Alternate Domains

At present, most sensors operate in the frequency (spectral) domain. However, infrared data are collected in the time domain, and other time-domain sensors, including pulsed NMR, Fourier-transform ultraviolet-visible spectroscopic sensors are being studied for use as flow sensors. Processing sensor data in the time domain would greatly speed the analysis step, since the need for data transformation, however fast, can be circumvented. Other motivations for data analysis in alternate domains concern application of flow theory. Flow systems, like other diffusion-based phenomena, often have theoretical relations which are better solved in the Laplace domain.

Work in this area has concentrated on linear filtering of interferometric data from infrared observations of mixtures. A detailed examination of the advantages and disadvantages of filtering in the Fourier-domain was made. For comparison, a multivariate method often used in the frequency domain, the K-matrix calibration method, was applied in the frequency and Fourier domains. Both the K-matrix and Kalman filter methods were tested on simulated spectra, on real interferograms collected from mixtures examined by infrared spectroscopy, and on interferograms produced from Fourier or Hartley

transformation of visible - ultraviolet spectra collected on a conventional, diode-array instrument.

For simulated data with 3 to 7 components, as few as 125 points need be processed by the Fourier-domain filter to produce results equivalent to K-matrix regression on the full, 2048 point frequency-domain spectrum. This 16-fold decrease in the amount of data required to obtain concentration estimates translates to over a 16-fold increase in the speed of data processing, since the transformation from interferogram to spectrum may also be omitted. This increase in data processing speed may be used to increase the effective scan rate, permitting observation of transient species or faster kinetics with the same infrared spectrometer.

Fourier-domain analysis also offers other benefits. Perturbation of spectra - through small shifts (5 cm^{-1}) in peak locations - did not substantially degrade the Fourier domain analysis with the Kalman filter, although the frequency-domain analysis, using either the Kalman filter or the K-matrix regression, was substantially affected by these gross model errors. Upon more substantial perturbation (10 cm^{-1} shifts) the Fourier-domain-based Kalman filtering failed, but the estimated concentrations remained within one order of magnitude of the true answer, while frequency-domain methods and the K-matrix regression in the Fourier-domain were in error by several orders of magnitude. There are limits to the Fourier-domain analysis, of course. As the number of points analyzed decreases, Fourier-domain analysis using either the Kalman filter or K-matrix methods becomes less reliable, and concentration estimates diverge from the true answers. This corresponds to an analysis of data showing very poor spectral resolution; in this case, all mathematical methods must fail, eventually, because the spectral information required to estimate components is absent. Fourier-domain estimation also fails when a peak which is outside the useful dynamic range of the instrument occurs as part of a measured spectrum. In the Fourier domain, the error produced by this peak extends over many points in the interferogram, while in the frequency domain, the error is much more localized.

When these methods were applied to infrared spectra taken on mixtures, results similar to those reported above were observed. The resolution of n-pentane and decalin, two compounds with very similar infrared spectra, was studied as a function of resolution. When the full, 2048-point, single-scan interferogram was filtered, estimation errors of 3-4% were observed. Upon filtering the first 95 points of the interferogram, estimation errors increased to 6-9%. This amounts to 3-fold increase in the error for a decrease in resolution of 21-fold. Given the similarities between the spectra, even at full resolution, this result is remarkable. In fact, the estimation error only increases when the spectra become so similar that their condition number rises dramatically. As above, the ability to obtain useful estimates with a substantial decrease in resolution may be traded for equivalent estimation from interferograms taken with decreased scan time. Two publications reporting the details of these studies are now in press in *Applied Spectroscopy*.

The same methods were applied to ultraviolet spectra that were taken on solutions which contained a sizable scattering component, to determine whether Hartley domain analysis might be able to discriminate against the broad, intense signal produced by the scattering. For these studies, acidic solutions of copper and nickel were measured, then 5 nm alumina was added. When analyzed in the frequency domain, all mathematical methods were unable to produce satisfactory estimates due to the intense light scattering produced by the alumina. Analysis of the interferograms calculated from the visible spectra produced results which deviated from true concentrations by less than 5%, when the first 5 points of the interferogram were not filtered. This work is being prepared for submission to *Applied Spectroscopy*.

4. Factor Modeling Methods For Complex Chemical Systems

The calibrations methods reported in the literature and developed here all require some prior knowledge of the composition and the concentration of the analytes. Often, however, neither the identity nor the concentration of components is known for many systems, including many chemical reactions, some complex chemical equilibria. When the chemical model cannot be discerned before data collection, a calibration step cannot be performed. In these cases, factor analysis (11) may be helpful in identifying chemical models from variations in the data. In factor analysis the data, contained in a matrix, $\mathbf{D}$ are presumed to be described by the product of two abstract factor matrices, $\mathbf{R}$ and $\mathbf{S}$

$$\mathbf{D} = \mathbf{R}_{\text{abs}} \mathbf{S}_{\text{abs}} \quad (3)$$

This relation is especially convenient for spectra, since $\mathbf{D}$ can be taken as absorbance, $\mathbf{R}$ as concentration and $\mathbf{S}$ as the product of molar absorptivity and path length. Many workers have discussed factor methods for self-modeling of data, in order to obtain the true spectra of components, but the literature is limited to reports of methods for either two or three components. Most chemical systems of interest have more than two components, and an alternate method to those reported (11) is required. The problem is to rotate the abstract matrix $\mathbf{S}_{\text{abs}}$ obtained from the factor analysis to the true matrix $\mathbf{S}_{\text{true}}$; from linear algebra theory, both are equivalent representations of the data. Methods based on modifications of the well-known two-component solution of Lawton have seen increasing use to circumvent the difficulty of finding the proper rotation matrix needed to transform the abstract factors into the true spectral responses (11). These iterative methods require moderately well-resolved responses to start, conditions not often met in chemical kinetics or in flow injection.

We have considered the problem of finding the correct rotation in detail. A new method which we have developed, which is based on the minimization of the information entropy of trial spectra in $\mathbf{S}$, seems to offer significant advantages over the other methods. The entropy is used to decide the optimal rotation of eigenvectors of the data set; as noted above, a suitable combination of rotated eigenvectors must describe the true spectra (or other single-component response) of components which produced the observed data. With normalization, the factor problem becomes an n -dimensional rotation optimization problem for n components, and the minimum entropy permits location of n rotation optima. From these optima, the single-component responses are extracted. The principal advantage of this method is generality: in theory, as many components can be self-modeled through these rotations as are present in the data. Thus, the older limits to self-modeling curve resolution are no longer true. This work is now being submitted to the *Journal of Chemometrics*.

In practice, however, the minima describing the correct rotations are strongly affected by noise in the data. The noise propagates through the factor analysis, and alters the nature of the eigenvectors, leading to incorrect (and very noisy) estimated spectra. To address the problem of noise, we have discovered that Fourier-domain smoothing, optimized by selecting smoothing parameters so that the information entropy of the smoothed data is minimized, produces smoothed data with minimal distortion. A detailed study of this new method found that it is very robust, and, more significantly, that the smoothing produced by this method is almost identical to that achieved knowing the true peak shape in advance. This entropy-based smoothing is also very general: it can be used to optimize such diverse signal processing methods as boxcar averaging, the popular Savitsky-Golay polynomial smoothing, and even adaptive smoothing methods (12). We have used it here to decrease the noise in spectral data prior to factor analysis, and to decrease the noise in eigenvectors after factor analysis, but prior to the rotation discussed above. This smoothing is one key to extracting multiple spectral components by minimum-entropy factor rotation. This study has been submitted to *Analytical Chemistry*.

Using the entropy-based rotation and the entropy-based smoothing, we studied several systems in detail. The method is limited by noise and by correlation in the data to be modeled: highly similar spectra cannot easily be factor modeled. However, typical spectra are easily resolved, and as many as nine factors can be resolved from data with S/N ratios near 1000, after the smoothing discussed above. With moderately correlated data, it is necessary to restrict solutions to those having positive peaks and positive concentrations, a restriction that carries a penalty (as discussed above for the simplex-optimized adaptive filter work) and which has the undesirable side effect of producing multiple false minima. These false minima cause the most difficulty in reaching suitable solutions.

The method works well with real spectral data, despite the need to check each minimum found. As Figure 6 shows, a set of five spectra containing three components was resolved to the component spectra with little trouble. Those estimated spectra agree very well with the true spectra. For five components, a data matrix made from ten measured spectra was decomposed and rotated to produce estimated spectra which also agree well with those measured for the single components. The previous best for self-modeling of spectra was three components, a number achieved only with some difficulty. Resolution of five components was no more difficult than resolution of three components, as Figure 7 shows, and there is no reason to believe that more could not be done as easily.

It is also possible to rotate $\mathbf{R}_{\text{abs}}$, the matrix that describes concentrations. Normalization required to reduce the rotation problem to order n (rather than n^2) prevents our obtaining absolute concentrations, but relative concentration estimates will be available from the rotated $\mathbf{R}$ matrix. By rotation, concentration relations can be detected for kinetics or for equilibrium relations that hold through a titration, for example. The rotation of $\mathbf{R}$ using the minimization of entropy was tested on a synthetic system containing five species related by a complex equilibrium:

Species L was taken as spectroscopically silent, but all other species were presumed to contribute to the simulated spectra. The spectra were simulated from the stability constants for each of the metal complexes and the free ligand concentration $[\text{L}]$. Factor analysis and extraction of significant eigenvectors was done in the usual manner, and matrices $\mathbf{R}_{\text{abs}}$ and $\mathbf{S}_{\text{abs}}$ were generated. The rotation of $\mathbf{R}_{\text{abs}}$ produced the familiar "alpha" plot, which relates relative amounts of the M species as a function of free ligand concentration. The predicted alpha plot is shown in Figure 8, along with the one used to create the simulated data. The agreement is striking. This rotation was repeated for data obtained from titration of Ni(II) in dilute nitric acid with ethylenediamine. The reaction was chosen because complexation produces a color change which permits the observer to continue the titration until all Ni species are formed. It was also convenient because the Ni species are well-studied in this system. A set of 50 spectra were collected over the titration, and the methods discussed above were applied to these data. Rotation of $\mathbf{R}_{\text{abs}}$ produced the alpha plot shown in Figure 8. Here, since only total ligand added is known, the alpha plot that results shows relative amounts of M species as a function of total ligand. The similarity of this plot, collected at 35 °C with the alpha plot shown for the Ni(II) ethylenediamine

system, measured at 25 °C, is very good. With the rotation of R_{abs} comes the side benefit of a similar rotation of S_{abs} . In this case, rotation of S_{abs} produces the spectra of each of the three Ni(II) ethylenediamine complexes, as well as the spectrum of the Ni(II) aquo ion. These are shown in Figure 9, along with spectra obtained on pure complexes (13). Agreement with published spectra obtained on synthetically pure Ni(II) ethylenediamine complexes is very good. Thus, spectra and relative amounts of species have been deduced from a simple titration, where only the total ligand added was known. This method will certainly be very useful for unraveling species identities and concentration gradients in flow experiments, and it also may be suited to use in examination of surface interactions or in other experiments where species cannot be individually studied. One particularly attractive application suggested by these studies is metal speciation, because there are many situations where, for whatever reason, individual metal-ligand complexes cannot be separated, and fundamental studies of speciation hang on the separation and identification of the species present in mixtures of metal and ligands.

Finally, it should be noted that the factor rotation method can be applied to many other systems. One such system is the examination of reacting systems. Over the past year, it has been extended, and coupled with rank annihilation methods, to permit the multivariate analysis of mass spectral measurements made on a transient mixture from pyrolysis of bacteria. The mass spectral signatures of the components of this complex mixture were identified and their time profiles were obtained through a series of entropy-based rotations and rank annihilations.

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6. Captions for Figures

Figure 1: Interaction of nicotinic acid with hydroxide at the bolus-carrier interface

A: Spectral data collected over the bolus.

B: Species distributions across the bolus.

Figure 2: Use of General Simulation to Fit Non-Conventional Diffusion problems

A.

Top: Applied potential for square-wave voltammetry.

Bottom: Kalman filter-optimized fit of simulation to square-wave voltammetric response

B.

Top. Pseudo- random waveform used to excite electrified interface

Bottom. Kalman filter - optimized fit of digital simulation response to electrochemical data.

Figure 3: Error surfaces for Simulations of Cottrell and Nicholson-Shain responses

A. Cottrell response. Error surface of simulated versus analytic response is shown as a function of time and potential step.

B. Linear sweep voltammetric response. Error surface of simulated versus Nicholson-Shain tabulated values of the dimensionless current as a function of potential.

Figure 4: Response surface for Trace, Area and Entropy metrics in Simplex-optimized Adaptive filtering.

A: Trace metric, with corresponding error surface (shows error in estimation for each point on the optimization surface).

B: Area metric, with corresponding error surface.

C: Entropy metric, with corresponding error surface.

Figure 5: Correction of linear and proportional drift by Kalman filtering

A: Correction of linear drift data. Noisy, drift-corrupted data are shown, along with Kalman filter estimates and, for comparison, least-squares estimates.

B: Correction of proportional drift data. Noisy, drift-corrupted data are shown, along with Kalman filter and least squares estimates of concentrations.

Figure 6: Spectral data and extracted components from factor rotation.

A: Three-component spectral data subjected to analysis

B: Extracted spectra, with true spectra (measured on individual components) for comparison

Figure 7: Factor rotation of concentrations to discover concentration relations. A five-component equilibrium system was studied by factor modelling.

A: Theoretical concentration relations and simulated spectra used to create simulated data for analysis.

B: Factor-rotated solutions for concentration relations and spectra of the components underlying the simulated data.

Figure 8: Factor rotation of titration data. Plots of the fractional concentration of Ni(II) species as a function of total ethylenediamine.

A: Factor-rotated solution, for data collected at 35 C.

B: Theoretical relation, calculated from stability constants measured at 25 C.

Figure 9: Factor-Rotated Spectra Obtained for the Ni(II) ethylenediamine system from titration data.

A: Factor -rotated spectra

B: Spectra taken from reference 13.

A

B

Figure 1

Figure 2 A

Figure 2B

A. Simulation Error Surface For Cottrell Experiment

B. Simulation Error Surface for Linear Sweep Voltammetry

Figure 3

Figure 4

Figure 5A

Figure 5B

Figure 6

A

B

Figure 7

Figure 8

A.

B.

Figure 9

7. Research Papers Published and/or Submitted from DOE Supported Research

1. Chemical Measurements and Data Reduction from a Systems Analysis Perspective, *TrAC*, 6(10) 260-266 (1987).
2. Kalman Filtering of First-Order Chemical Kinetics using Fourier Transform Infrared Spectroscopic Data, *Anal. Chim. Acta*, 200, 397-410 (1987). (with S.L. Monfre).
3. Multicomponent Analysis in Static and Flow Systems using Digital Filters, *NBS J. Research*, 93, 253-5 (1988). (with T.Q. Barker, H.R. Wilk and S.L. Monfre).
4. Estimation of Second-Order Kinetic Parameters Using the Extended Kalman Filter, *J. Chemometrics*, 2, 137-154 (1988). (with T.Q. Barker).
5. Chemometrics: Fundamental Review, *Anal. Chem.*, 60, 252-274R (1988). (with T.Q. Barker, R.A. Larivee, S.L. Monfre, and H. Wilk).
6. Analysis of a Coeluting Chromatographic Pair in Liquid Chromatography, *J. Chromatography*, 469, 77-90 (1989). (with T.Q. Barker).
7. Modifications to the Simplex-Adapted Kalman Filter, *Anal. Chim. Acta*, 225, 37-53 (1989). (with H.R. Wilk).
8. Analysis of Partially Resolved Liquid Chromatographic Peaks by using Dynamic Modelling with the Kalman Filter, *Anal. Chim. Acta*, 225, 53-69 (1989). (with T.Q. Barker).
9. Qualitative and Quantitative Analysis of Unresolved Responses in Liquid Chromatography with Fourier Transform Infrared Spectroscopic Detection, *Anal. Lett.*, 22, 963-981 (1989). (with M. Redmond and H.R. Wilk).
10. Quantitative Fourier-Domain Analysis. Part 1: Analysis of Raw FTIR Interferograms, *Applied Spectroscopy*, accepted for publication (1991). (with S.L. Monfre).
11. Quantitative Fourier-Domain Analysis. Part 2: Determination of Boundary Conditions, *Applied Spectroscopy*, accepted for publication (1992). (with S.L. Monfre).
12. Rapid Parameter Estimation with Incomplete Chemical Calibration Models, *Chemom. Int. Lab. Systems*, 10, 87-105 (1992).
13. Smoothing of Noisy Data by Minimization of Cross-Spectral Entropy, *Anal. Chem.*, submitted for publication (1991). (with R. Larivee)
14. Principal Component Modelling of Overlapped Spectra by Minimization of Cross-Spectral Entropy, *J. Chemometrics*, submitted for publication (1992). (with R. Larivee)
15. Innovations-variance Adaptive Filtering for Quantitative Analysis with Incomplete Calibration Models. *Anal. Chim. Acta*, submitted for publication (1992). (with H. Wilk)

16. Quantitative Analysis of Polar Organic Mixtures by Infrared Spectroscopy and Digital Filtering, Anal. Chim. Acta, submitted for publication (1992). (with H. Wilk)

17. Chemometrics: Fundamental Review, Anal. Chem., 62, 84R-101R (1990).

18. Real-Time Filtering of Data from Mobile, Passive Remote Infrared Sensors with Principal Component Models of Background, J. Chemometrics, 5, 147-161 (1991).

19. Partial Least Squares Regression For Mass Spectral Analysis Of H₂ And D₂ Scrambling Products, Industrial and Engineering Chemistry, in press, (1992). (with S. Sengupta and H. Foley)

20. Chemometrics: Fundamental Review, Anal. Chem., accepted for publication (1992). (with R.S. Bear and T.B. Blank)

21. Fuzzy Kalman Filtering, Anal. Chim. Acta, to be submitted for publication (1992) (with S.J. Stuart).

Chapters and Books

22. Signal Analysis: Correlation and Time Series Analysis, IUPAC Monograph on Chemometrics, in press, 1992.

23. Multicomponent Analysis and Chemometrics for Bioprocess Control, in "Sensors in Bioprocess Control", J. Twork and A. Yacynych, Eds., Marcel Dekker, New York, NY, 1990, Chapter 12.

24. Signal Processing, in "Practical Guide to Chemometrics", S.J. Haswell, ed., Marcel Dekker, New York, 1992, Chapter 8.

25. The Future of Chemometrics, in "Practical Guide to Chemometrics," S.J. Haswell, ed., Marcel Dekker, New York, 1992, Chapter 10.

26. Summation of "Tensorial Calibration I and II", by E. Sanchez and B.R. Kowalski, Chemtracts, 1, 319-321 (1989).

27. Book Edited: "Sequential Simplex Optimization", by F. Walters, L. Parker, S. Morgan and S. Deming, published by CRC Press: Boca Raton, FL, 1991.

8. Invited Seminars and Talks Presented

1. "Digital Filters in Multicomponent Chemical Analysis", E.I. DuPont Co., Wilmington, DE, July, 1987.

2. "Digital Filters for Kinetic Analysis in Flow Systems", Eastern Analytical Symposium, New York, NY, September, 1987.

3. "Multicomponent Analysis in Static and Flow Solution", NBS Conference on Trace Analysis, Gaithersburg, MD, September, 1987.

4. "New Approaches in Kinetic Analysis", Seton Hall University, E. Orange, NJ, October, 1987.

5. "Optimization of Digital Simulations using the Extended Kalman Filter", Scientific Computing Conference, Atlantic City, NJ, November, 1987.
6. "Multicomponent Analysis without Separations", Eastman Kodak Co., Rochester, NY, December, 1987.
7. "Real-Time Multicomponent Analysis using the Kalman Filter", CAC88, Amsterdam, The Netherlands, May, 1988.
8. "Digital Filtering for Chemical Analysis and Modelling", Technical University of Vienna, Vienna, Austria, June, 1988.
9. "Real-Time Chemical Analysis of Transient Samples using Digital Filtering Methods", Technical University of Graz, Graz, Austria, June, 1988.
10. "Curve Resolution and Purity Determination of Poorly Resolved Chromatographic Peaks Using Kalman Filtering", 12th International Symposium on Column Liquid Chromatography, Washington, DC, June, 1988.
11. "Real-Time Analysis of Mixtures using Digital Filters", Department of Chemistry, Villanova, PA, September, 1988.
12. "Robust Adaptive Filtering of Infrared Spectra for Real-Time Multicomponent Analysis", Eastern Analytical Symposium, New York, NY, October, 1988.
13. "Real-Time Multicomponent Analysis using the Kalman Filter", FACSS Conference, Boston, MA, October, 1988.
14. "Getting Something for Nothing: Mixture Analysis using Digital Filters", Mobil Research and Development Corporation, October, 1988.
15. "Real-Time Multicomponent Analysis using the Kalman Filter", Princeton Applied Research Corp., Princeton, NJ, November, 1988.
16. "Characterization of Mixtures using Factor Analysis and Minimum Entropy", FACSS Conference, Chicago, IL, October, 1989.
17. "Rapid Parameter Estimation using Incomplete Calibration Models," Mathematics In Chemistry Conference, College Station, TX, November, 1989.
18. "Chemometric Methods for Qualitative and Quantitative Analysis of Complex Mixtures," University of Maryland, College Park, MD, November, 1989.
19. "Applications of Chemometric Methods in Analytical Chemistry," Hercules Chemical Co., Wilmington, DE, November, 1989.
20. "Getting Something for Nothing: Analytical Chemistry in the Absence of Information," Pennsylvania State University, University Park, PA, December, 1989.
21. "Analytical Chemistry in the Absence of Prior Information", University of Alaska, Anchorage, AK, March, 1990.

22. Tensorial Calibration (Invited Discussant), Gordon Conference on Mathematics and Statistics in Chemistry and Chemical Engineering, New Hampton School, NH, July, 1990.
23. "Qualitative and Semi-quantitative Analysis of Poorly-Defined Mixtures", SCA Conference, Philadelphia, PA, September, 1990.
24. "Digital Filtering with Incomplete Signal Information", FACSS Conference, Cleveland, OH, October, 1990.
25. "Qualitative and Semi-quantitative Analysis of Poorly-Defined Mixtures", Lebanon Valley College, Annville, PA, October, 1990.
26. "Applications of Digital Filtering," EPA Conference on Chemometrics and Statistics, Las Vegas, NV, November, 1990.
27. "Digital Filtering with Incomplete Signal Information", Alcoa Aluminum Company, Pittsburgh, PA, November, 1990.
28. "Digital Filtering with Incomplete Signal Information", DuPont Company, Wilmington, DE, November, 1990.
29. "Qualitative and Semi-quantitative Analysis of Poorly-Defined Mixtures", ATOChem North America, King of Prussia, PA, November, 1990.
30. "Qualitative and Semi-quantitative Analysis of Poorly-Defined Mixtures", ICI Pharmaceuticals, Wilmington, DE, December, 1990.
31. "Real-Time Analysis of Passive Remote Infrared Data by Recursive Digital Filtering", Dickinson College, Carlisle, PA, February, 1991.
32. "Getting Something for Nothing in Chemistry", SAS Lecture, Louisiana Section, New Orleans, LA, April, 1991.
33. "Real-Time Analysis of Passive Remote Infrared Data by Recursive Digital Filtering", Emory University, Atlanta, GA, April, 1991.
34. "Getting Something for Nothing in Chemistry", SAS Lecture, Piedmont Section, Atlanta, GA, April, 1991.
35. "Qualitative and Semi-quantitative Analysis of Poorly-Defined Mixtures", Drexel University, Philadelphia, PA, May, 1991.
36. "Adaptive Kalman filtering of Infrared Spectra", Chemometrics in Analytical Chemistry (CAC-V), Montreal, Canada, July, 1992.
37. "Fuzzy Kalman Filtering", Computer Applications in Analytical Chemistry (COMPANA), Jena, Germany, August, 1992 (Plenary Lecture).
38. "Adaptive Kalman Filtering", FACSS, Philadelphia, PA, September, 1992.

9. Contributed Talks at Conferences, etc.

39. "Digital Filtering in Flow Solution", National Meeting of the ACS, New Orleans, LA, September, 1987.

40. "Kalman Filtering in Alternate Domains", FACSS, Detroit, MI, October, 1987.

41. "Examination of Complex Equilibria using Kalman Filtering and Minimum Entropy", Pittsburgh Conference on Analytical Chemistry, New Orleans, LA, February, 1988.

42. "Multicomponent Analysis using Fuzzy Set Theory and the Kalman Filter", Pittsburgh Conference on Analytical Chemistry, New Orleans, LA, February, 1988.

43. "HPLC Curve Resolution and Peak Purity Determination using the Kalman Filter and Photodiode Array Detection", Pittsburgh Conference on Analytical Chemistry, New Orleans, LA, February, 1988.

44. "Kalman Filtering in Alternate Domains", Pittsburgh Conference on Analytical Chemistry, New Orleans, LA, February, 1988.

45. "Real-Time Chemical Analysis using the Kalman Filter", Pittsburgh Conference on Analytical Chemistry, New Orleans, LA, February, 1988.

46. "Improved Adaptive Kalman Filters", Pittsburgh Conference on Analytical Chemistry, New Orleans, LA, February, 1988.

47. "Fuzzy Calibration", Mid-Atlantic Regional Analytical Chemistry Conference, Potsdam, NY, October, 1988.

48. "Real-Time Chromatographic Analysis using Recursive Digital Filtering", Pittsburgh Conference on Analytical Chemistry, Atlanta, GA, March, 1989.

49. "Parameter Estimation in the Fourier Domain", Pittsburgh Conference on Analytical Chemistry, Atlanta, GA, March, 1989.

50. "Optimal Fourier Smoothing of Spectra using Minimum Entropy", Pittsburgh Conference on Analytical Chemistry, Atlanta, GA, March, 1989.

51. "A Robust, Adaptive Kalman Filter for Real-Time Analysis", Pittsburgh Conference on Analytical Chemistry, Atlanta, GA, March, 1989.

52. "Nonlinear Calibration" (Poster), Pittsburgh Conference on Analytical Chemistry, Atlanta, GA, March, 1989.

53. "Knocking the Rough Edges off Data with Entropy," Mid-Atlantic Regional Analytical Chemistry Conference, Villanova, PA, October, 1989.

54. "Optimizing Digital Simulations of Voltammetry with Recursive Digital Filters", MARM, Newark, DE, May, 1991.

56. "Investigation of Systematic Errors in Electrochemical Simulations", FACSS, Philadelphia, PA, September, 1992.

10. Student and Other Researchers Participating on DOE -Supported Projects

Visiting Faculty

Professor Marylynn Grayeski, Department of Chemistry, Seton Hall University. Prof. Grayeski worked on modelling of solution reactions and adaptive filtering of overlapping responses during a sabbatical visit to Delaware.

Graduate Students

1. Molly A. Redmond (M.S., 1988, University of Delaware).
Thesis Title: Multicomponent Analysis of Mixtures by LCIR with Kalman Filtering.
Ms. Redmond is presently on the research staff, Oxychem, Houston TX.
2. Harlan L. Wilk (Ph.D., 1989, University of Delaware)
Thesis Title: Novel Methods for Adaptive Kalman Filtering
Dr. Wilk is presently on the research staff, Goodyear, Inc., Akron, OH.
3. Robert J. Larivee (Ph.D., 1989, University of Delaware)
Thesis Title: New Methods of Factor Analysis
Dr. Larivee is presently Assistant Professor, Frostburg State University, Frostburg, MD.
4. Todd Q. Barker (Ph.D., 1991, University of Delaware)
Thesis Title: Analysis of Transient Chemical Species in Analytical Chemistry using the Kalman Filter.
Dr. Barker is presently on the research staff, Baxter HealthCare, Miami, FL.
5. Stephen L. Monfre (Ph.D., 1991, University of Delaware)
Thesis Title: Kalman Filtering in Alternate Domains
Dr. Monfre is presently manager of applications, Peristorp-NIRSystems, Silver Spring, MD.
6. Robert S. Bear, Jr. (Ph.D. expected 1993, University of Delaware)
Mr. Bear is a graduate student at the University of Delaware. His Ph.D. thesis concerns the modelling of heterogeneous kinetics by digital simulations.
7. Thomas B. Blank (Ph.D. expected 1994, University of Delaware)
Mr. Blank is a graduate student at the University of Delaware. His Ph.D. thesis concerns nonlinear calibration and multicomponent analysis of mixtures where incomplete calibration information is available.

Undergraduate Students

1. Steven J. Stuart (B.S. (Hons.) 1990, University of Delaware) worked on applications of fuzzy filtering to kinetic analysis.
Thesis Title: Application of Fuzzy Set Theory to Curve Fitting.
Mr. Stuart is presently an NSF fellow in Ph. D. program in Theoretical Chemistry, Columbia University, New York City, NY.

2. Bernice E. Yeung (B.S., 1988, University of Delaware) assisted with interfacing work. Ms. Yeung is presently attending graduate school at Northeastern University, Boston, MA.
3. Joseph Shane (B.S., 1991, University of Delaware) assisted with some spectroscopic studies. Mr. Shane is presently attending graduate school at Purdue University, West Lafayette, IN.

END

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