decision making, such that it could direct an experimental investigation and provide an interpretation of results. This software would operate on a "dynamic" data set, because it would order new experimental results on the basis of prior results and its own working hypothesis. Early versions would certainly have expert character; hence, we term them "dynamic expert systems" in order to distinguish them from expert systems that operate on invariant data that they have no part in gathering.

Eklund has actually developed a dynamic expert system for electrochemistry.[35] He developed his software on a VAX 11/780 to operate a cybernetic potentiostat like the one described earlier in this article, and it used a multitechnique approach to the investigation of three chemical issues: the stability of a product of an electrode reaction, the *n* value of an electrode reaction, and diffusion control of the current. The operator would simply define the issue of interest; then, the VAX would direct the cybernetic potentiostat through a series of cyclic voltammetric and chronocoulometric experiments bearing on the issue of interest. The results were compared with ideal responses, and a voting technique was used to provide a conclusion.

The degree of chemical "expertness" embodied in Eklund's system was relatively low. It did not engage in experimental protocols extending beyond a couple of techniques, and it did not formulate hypotheses for testing with further experiments. Nevertheless, his achievement was substantial, because he provided a general solution to the problem of interinstrument communication by text commands and he developed data structures that are particularly well suited to dynamic expert systems. Basically his research has provided a vision of the kinds of things that one might accomplish with an expert system operating with an instrument capable of an extensive experimental repertoire. Impressive developments of this idea are bound to follow.

An important prerequisite is a set of diagnostics by which decisions can be made. Since the decisions are to rest on a machine, then the diagnostics must be numeric. Therdteppitak and Maloy have begun to address the systematic development of diagnostics, and they have suggested that the exponent on the time variable will be particularly valuable as a means for distinguishing the rate-controlling elements in an electrochemical process.[36] In the end, the utility of any expert system, static or dynamic, will depend on the reliability of its diagnostics. The serious exploration of new diagnostics is critical to any significant application of artificial intelligence in electrochemistry.

ACKNOWLEDGMENT

We are grateful to the National Science Foundation for supporting this work under Grant CHE-81-06026.

REFERENCES AND NOTES

(1) Anson, F. C. *Anal. Chem.* **1966**, *38*, 54.
(2) Lauer, G.; Abel, R.; Anson, F. C. *Anal. Chem.* **1967**, *39*, 765.
(3) Osteryoung, J. *Science (Washington, D.C.)* **1982**, *218*, 261.
(4) Lauer, G.; Osteryoung, R. A. *Anal. Chem.* **1968**, *40* (10), 30A.
(5) Turner, J. A.; Christie, J. H.; Vukovic, M.; Osteryoung, R. A. *Anal. Chem.* **1977**, *49*, 1904.
(6) Osteryoung, J. G.; Osteryoung, R. A. *Anal. Chem.* **1985**, *57*, 101A.
(7) Schwall, R. J.; Bond, A. M.; Loyd, R. J.; Larsen, J. G.; Smith, D. E. *Anal. Chem.* **1977**, *49*, 1797.
(8) Anderson, J. E.; Bond, A. M. *Anal. Chem.* **1981**, *53*, 1394.
(9) He, P.; Avery, J. P.; Faulkner, L. R. *Anal. Chem.* **1982**, *54*, 1313A.
(10) He, P. Ph.D. Thesis, University of Illinois at Urbana-Champaign, 1985.
(11) Smith, D. E. In "Fourier, Hadamard and Hilbert Transforms in Chemistry"; Marshall, A. G., Ed.; Plenum Press: New York, 1981.
(12) Creason, S. C.; Smith, D. E. *Anal. Chem.* **1973**, *43*, 2401.
(13) deLeeuwe, R.; Sluyters-Rehbach, M.; Sluyters, J. H. *Electrochim. Acta* **1969**, *14*, 1183.
(14) Rohko, T.; Kogoma, M.; Aoyagui, S. *J. Electroanal. Chem.* **1972**, *38*, 45.
(15) Hayes, J. W.; Glover, D. E.; Smith, D. E.; Overton, M. W. *Anal. Chem.* **1973**, *45*, 277.
(16) O'Halloran, R. J.; Smith, D. E. *Anal. Chem.* **1978**, *50*, 1391.
(17) Grabaric, B. S.; O'Halloran, R. J.; Smith, D. E. *Anal. Chim. Acta* **1981**, *133*, 349.
(18) (a) Oldham, K. B. *Anal. Chem.* **1972**, *44*, 196. (b) Imbeaux, J. C.; Saveant, J.-M. *J. Electroanal. Chem.* **1973**, *44*, 169.
(19) Soong, F.-C.; Maloy, J. T. *J. Electroanal. Chem.* **1983**, *153*, 29.
(20) Feldberg, S. W. *Electroanal. Chem.* **1969**, *3*, 199.
(21) Maloy, J. T. In "Laboratory Techniques in Electroanalytical Chemistry"; Kissinger, P. T.; Heineman, W. R., Eds.; Marcel Dekker: New York, 1984; pp 417-462.
(22) Pons, S. *Electroanal. Chem.* **1984**, *13*, 115.
(23) Sybrandt, L. B.; Perone, S. P. *Anal. Chem.* **1972**, *44*, 2331.
(24) Pichler, M. A.; Perone, S. P. *Anal. Chem.* **1974**, *46*, 1790.
(25) Thomas, Q. V.; Perone, S. P. *Anal. Chem.* **1977**, *49*, 1369.
(26) Thomas, Q. V.; DePalma, R. A.; Perone, S. P. *Anal. Chem.* **1977**, *49*, 1376.
(27) DePalma, R. A.; Perone, S. P. *Anal. Chem.* **1979**, *51*, 825.
(28) DePalma, R. A.; Perone, S. P. *Anal. Chem.* **1979**, *51*, 839.
(29) Schachterle, S. D.; Perone, S. P. *Anal. Chem.* **1981**, *53*, 1672.
(30) Burgard, D. R.; Perone, S. P. *Anal. Chem.* **1978**, *50*, 1366.
(31) Byers, W. A.; Freiser, B. S.; Perone, S. P. *Anal. Chem.* **1983**, *55*, 620.
(32) Jurs, P.; Isenhour, T. "Chemical Application of Pattern Recognition"; Wiley: New York, 1975.
(33) Wilkins, C. L.; Jurs, P. C. In "Transform Techniques in Chemistry"; Griffiths, P. R., Ed.; Plenum Press: New York, 1978.
(34) Kowalski, B. R.; Bender, C. F. *J. Am. Chem. Soc.* **1972**, *94*, 5632.
(35) Eklund, J. A., Ph.D. Thesis, University of Illinois at Urbana-Champaign, 1984.
(36) Therdteppitak, A.; Maloy, J. T. *Anal. Chem.* **1984**, *56*, 2594.

Microelectronics in Analytical Chemistry

RAYMOND E. DESSY
Chemistry Department, Virginia Polytechnic Institute and State University, Blacksburg, Virginia 24061

Received February 19, 1985

Although small computer systems have impacted the practice of analytical chemistry by their ability to help capture and electronically manipulate data in traditional ways, even greater effects of this microelectronic revolution are becoming apparent. First, microelectronic fabrication techniques are being used to make new classes of transducers. Second, new integrated circuits are being developed that allow the chemist to correlate, convolve, and domain convert data both before and after capture by the computer. These front-end and back-end processing elements open up the world of small computers to techniques usually requiring large mainframe processors. Third, arrays of nonspecific sensors are being used that are based on solid-state detectors and chemimetric techniques. Finally, new classes of self-optimizing instruments are being created. Typical examples from each of these areas are presented.

Small computer systems and microelectronic components give the scientist a new set of tools for the laboratory. Increasing evidence shows many laboratories are beginning to use these tools to perform experiments in novel ways, often

0095-2338/85/1625-0282$01.50/0

Raymond E. Dessy is Professor of Chemistry at Virginia Polytechnic Institute and State University. His research group is currently interested in computer automation of instruments, the design of new types of detectors, new methods for data acquisition and handling, and more effective ways to teach chemists about computers and laboratory automation. He began teaching at the University of Cincinnati in 1957, and in 1966 he came to VPI & SU and continued research in organometallic electrochemistry and fast-reaction mechanisms. The computer was a logical step in the search for new and faster ways to detect, acquire, and process data. His B.S. in pharmacy in 1953 and his Ph.D. in chemistry in 1956 were from the University of Pittsburgh, followed by a postdoctoral fellowship with Mel Newman at The Ohio University. He was a Sloan Fellow from 1962 to 1964, was past Chairman of the ACS Computer Division, and is an ACS tour speaker since 1969. He is Editor of the A/C Interface column, which has appeared in *Analytical Chemistry* since 1982. He is Chairman-elect of the Laboratory Automation Subsection of the ACS Computer Division.

undertaking studies precluded by classical methods. Using new tools requires an understanding and mastery of them, and microelectronics is no exception.

Typical applications of these new servants to the instrument environment will be described. Design goals and concepts are the focus rather than the specific chemistry involved. The ensemble is meant to give scientists some insight into ways to use these versatile tools in their research. The examples cited are not unique, nor necessarily the most elegant and sophisticated. Most are a collection of applications developed by members of the Laboratory Automation and Instrument Design Group at Virginia Polytechnic Institute and State University.

The exploration will start at the analytical transducer. The same solid-state electronics that make computers possible offer the potential for development of new transduction tools. This will be followed by several case histories involving data collection and interpretation, since the best use of laboratory computers often involves data-manipulation techniques that are foreign to the computer novice. Then some design considerations involved in a self-optimizing instrument will be presented.

THE LABORATORY ENVIRONMENT

The environment for the instrument developments to be described involves a network of synergistically interacting computers of various sizes. Each researcher in the Laboratory Automation and Instrument Design Group has a laboratory bench workstation with a basic configuration consisting of a 16-bit central processing unit (CPU) with microcoded math capabilities, a 16-channel 12-bit successive approximation

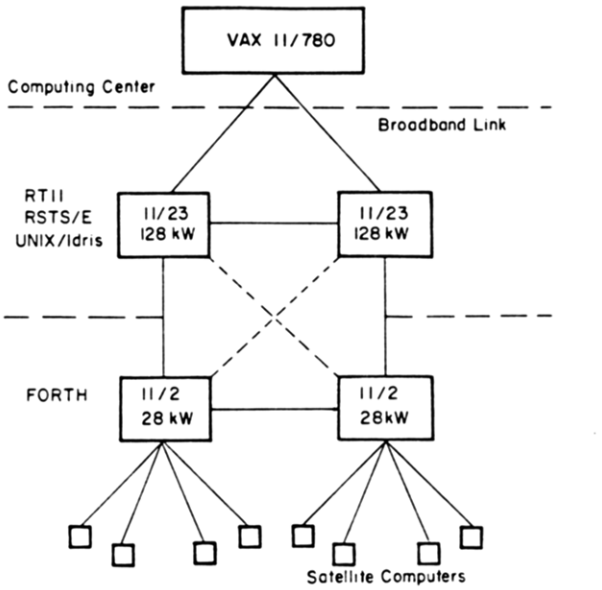

Figure 1. Laboratory computer network. All linkages support 9600 bits/s asynchronous communication.

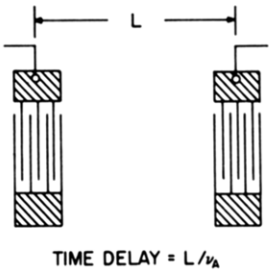

Figure 2. Typical surface acoustic wave (SAW) transducer.

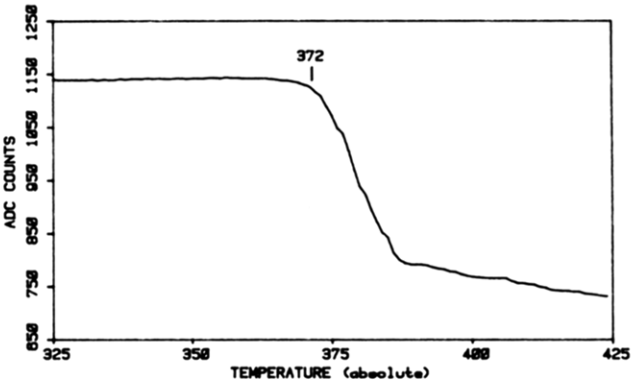

Figure 3. Thermogram of polymer sample made with a SAW device: thin-film glass transition in polystyrene.

analog-to-digital converter (A/D) subsystem (30-μs conversion time), dual 12-bit digital-to-analog converters (D/A's), four real-time clocks, and several serial and parallel input/output (I/O) ports. Each satellite processor is attached to one of two identical disk-server hosts via a 9600 bits/s RS-232 asynchronous communication line. All of the computers at this level are programmed in a concurrent indirectly-threaded code operating language called FORTH.

Each of the disk-server hosts can be connected to one of two identical general-purpose minicomputers with larger memory, rigid disks, and 64-bit integer and floating math implemented by microcode. These systems run a variety of operating systems such as RSTS-E, RT-11/TSX-PLUS, UNIX, or IDRIS. Each operating system, like the languages it supports, has different strengths and weaknesses.

The minicomputers are interconnected by a broad-band local area network (LAN) to the University IBM 370 and DEC

VAX facilities. Intercommunication and transfer through this four-level hierarchy is facile and often transparent to the user (Figure 1).

SOLID-STATE TRANSDUCERS

SAW Devices. Surface Acoustic Wave (SAW) devices (Figure 2) involve the laying down of an array of metallic finger pairs on a piezoelectric substrate. The electrodes are typically aluminum, and the substrate is quartz or lithium niobate. The application of RF energy in the megahertz region to the electrodes results in a surface propagating wave that involves retrograde elliptical motion of the ions in the crystal lattice. These waves can interact with gases or solids on the surface, affecting the amplitude of the wave, its frequency, or its phase shift. Originally developed for military applications, the typical SAW device has an equivalent set of finger pair electrodes at opposite ends of the substrate. One serves as the transmitter, the other as a receiver. This arrangement serves to make ideal tunable delay lines and filters for telecommunications.

Since SAW devices "drift" when exposed to ambient atmospheres, the electronics industry normally encapsulates them in inert gas containers. Exposed to gas chromatographic effluents or thin polymer films, they also make ideal chemical transducers. As a GC detector, they exhibit a high sensitivity but low dynamic range, making them suitable for process-control detection systems.

If thin polymer films are ramped in temperature from liquid nitrogen to melting point levels, SAW devices can detect low-order, glass, and melting transitions (Figure 3). Diffusion of gases into the polymer can be monitored at a fixed temperature by watching the diminution in amplitude or change in frequency of the SAW wave as the gas effects the polymer thermoelastic properties.[1,2] This is a brief example of how a solid-state electronic device can be modified to serve chemical applications. Many others exist.

Nonspecific Array Sensors. Doped tin oxide structures operating at elevated temperatures show a resistance that is a marked function of gases in the environment. First constructed as devices to detect hydrocarbon vapors in boat compartments, they offer the nucleus for an array of nonspecific array sensors. The breathing air in a typical fighter aircraft can be contaminated by a number of known materials. Acrolein (gasket decomposition), phthalate esters (plasticizers), and fuel components are typical contaminants.

Slight chemical modification to the SnO detectors changes the basic detector's response to each of these contaminents. A different chemical modification leads to a different set of response factors. Six modified sensors, each nonspecific, can serve as an array detector for four components. An oversolved set of simultaneous equations is involved.[3] Although these data would not be given to a technician to manipulate, it is a simple matter for a small microcomputer to produce a set of concentrations from the data set. As the problems in analytical laboratories escalate, more use will be made of nonspecific array detectors, coupled to computers, to extract useful information from multiple sensor responses.[4]

Discrete Optical Arrays. An example tying both of these concepts together involves a solid-state device to elicite size and distribution information from a flowing stream containing latex particles. Ten individual silicon photodiodes (1 mm × 1 mm) can be laid down in one integrated circuit (IC) carrier. Each photodiode is then overlaid by a different 10-nm bandpass interference filter. Finally, a mask is put in place and the device encapsulated with optical epoxy (Figure 4). The result is an array of filter photometers. Light scatter from the flowing stream can be monitored at multiple wavelengths by this IC detector. Once again, an oversolved set of equations

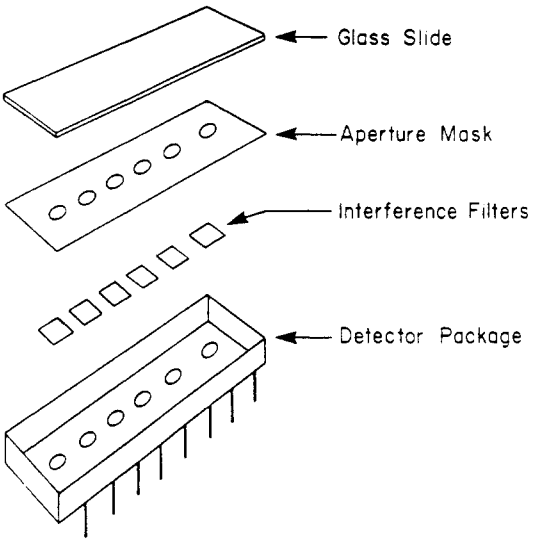

Figure 4. Fabrication of a discrete array of filter photometers.

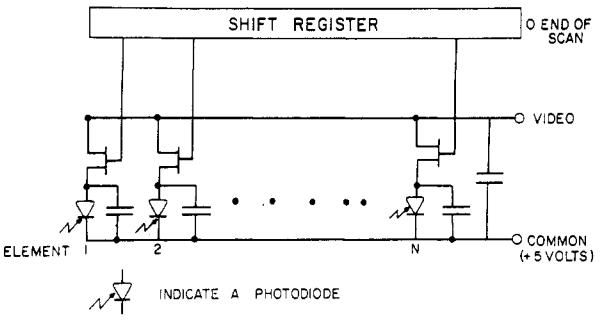

Figure 5. Architecture of a linear silicon photodiode linear array.

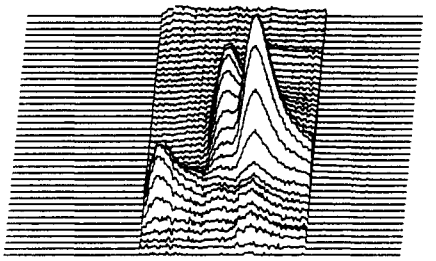

Figure 6. Three-dimensional data set (wavelength vs. absorbance vs. elution time) from a linear array LC detector.

exists that permits evaluation of particle size and distribution. With a hydrodynamic chromatography column in front of the flow cell, the system has successfully analyzed polydisperse samples.[5]

Linear Arrays. Discrete arrays complement the linear arrays that have revolutionized optical spectroscopy. Linear arrays have 256–1024 optically sensitive elements on one IC carrier. They are laid down by photolithographic techniques and involve charge-transfer or bucket-brigade technology. Light from an analytical source can be dispersed onto the array and the intensity in any pass-band area read electronically (Figures 5 and 6). The devices have been used to acquire spectra at 4000 spectra/s. In more prosaic applications, they have been used to collect 5–10 spectra/s of the effluent from a liquid chromatograph.[6-8] This allows the ancillary computer to determine whether an eluting peak is uniform. Identification from ultraviolet and visible spectra may be possible. It is possible to envisage spectrometers whose only moving parts are electrons and photons. Space missions have already demonstrated the application of acoustooptic and electrooptic devices for this purpose.

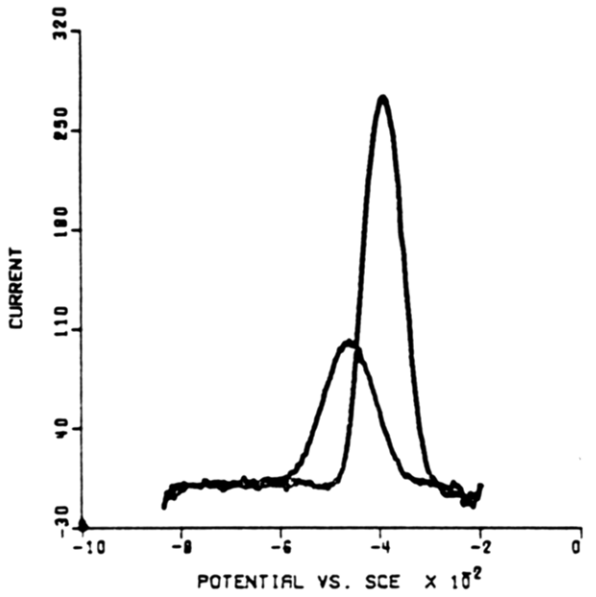

Figure 7. Typical decomposition of an overlapping set of electrochemical peaks done in the spatial frequency domain.

DATA MANIPULATION AND COMPRESSION

Fourier-Transform Methods. The extensive use of Fourier-transform (FT) techniques with nuclear magnetic resonance and infrared spectroscopy has made the scientist conversant with the basic principle involved. Data from an experiment is collected in one domain (e.g., time) and then converted to its reciprocal (e.g., frequency) for interpretation. The NMR experiment involves monitoring the free-induction decay curve from a set of perturbed nuclei over a very short time frame with high-speed A/D subsystem. The FT of the data gives a traditional frequency spectrum. The same approach is used in FT IR. However, FT techniques have a wider application.

Square-wave polarographic techniques apply a summed ramp/square-wave signal to an electrode. As the ramp is swept, the superimposed square wave alternately and rapidly cycles the material at the electrode through a redox cycle. The experiment is an ideal example of using the computer as a tool to produce the waveform required, as well as to monitor the current that flows at each applied potential level.

Interpretation of the curves that result from mixtures is often difficult. The decomposition process involved has usually been attacked by a linear parameter estimation (LPE) process. Unfortunately, this involves the manipulation of large arrays of information, e.g., 512 points for the unknown and each member of the decomposition set, covering a potential span of 2.56 V. It is possible to perform a Fourier transform on these data, converting it into the reciprocal domain. Studies show that only the first 10–20 spatial elements in this domain contain relevant information. The other 500–odd components can be ignored. Retransform will create a data set that is almost superimposable on the original data.

Even more pertinent, this reduced data set can be used to perform LPE calculations. The analytical results are identical with those derived from the temporal domain data set but involve manipulations of arrays that are vastly smaller (Figure 7). This allows even a small microcomputer to handle the LPE approach.[9]

Hadamard-Transform Methods. Fourier-transforms algorithms stress the computer, since extensive real number manipulations are involved, as well as sine/cosine functions. Compression of data from rapid scanning spectrophotofluorometers requires a different approach. These instruments, based on linear array or vidicon imaging devices, produce a fingerprint of a pure unknown material by creating a contour

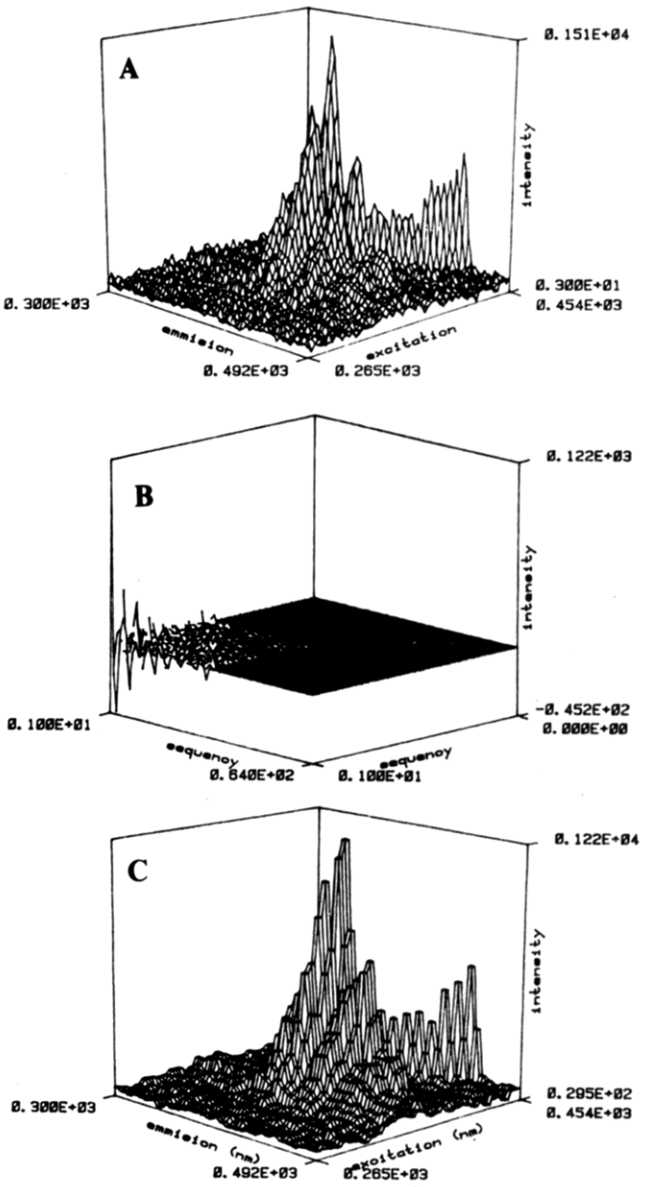

Figure 8. (A) original spectrophotofluorometer data set, (B) same set after Hadamard transform and discard of 75% of data, and (C) reconstructed set derived by *inverse* Hadamard transform of (B).

map relating exciting wavelength, emitted wavelength, and intensity. Spectral identification of a pure unknown with a library of knowns is hindered by the sheer mass of information. It is possible to convert this three-dimensional contour image into another domain.

Hadamard-transform functions offer some distinct advantages. Rather than analyze a complex waveform into a summation of sine and cosine functions, the Hadamard uses square-wave functions. Only multiplication and division by 2 is involved, simple operations for the microcomputer. Matrix symmetry further reduces computational load. Studies have shown that it is possible to convert spectrophotofluorometric 3-D information into the reciprocal Hadamard space and "throw away" 75% of the data. Retransform will generate a data set that is almost identical with the original. This means that the library searches conducted on reciprocal-space data involve minimal disk space, memory space, and time (Figure 8).[10]

Isenhour has demonstrated the applicability of FT compression techniques to mass spectral data. He has elegantly extended this by a clipping approach that further reduces the amount of stored information necessary for library search/match comparisons.[11] Increasingly, compression techniques

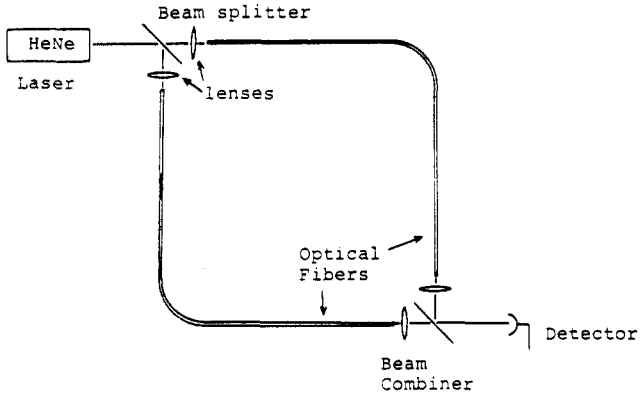

Figure 9. Mach–Zehnder interferometer.

such as these will be incorporated into instruments for all of the economies cited.

FRONT-END ELECTRONIC DATA ANALYSIS

Interferometer Phase-Shift Analysis. Single-mode fiber optics offer a platform upon which to build a variety of sensor types. Most of these are extrinsic, using the waveguides to plumb light around an instrument. A more exciting area involves instrinsic effects.

It is possible to construct a Mach–Zehnder interferometer from two pieces of single-mode fiber optics (Figure 9). The simplest approach twists the two fibers tightly together over a small distance, placing the waveguides in close proximity. An inexpensive helium/neon laser provides a coherent light source that is conducted into *one* of the fibers. The twisted, intimate section provides a "bottle coupler" that allows light to leak from one fiber to the other, giving the two arms of the interferometer a common coherent light signal to be transmitted.

If one arm of the interferometer has propagation characteristics that differ from the other due to length, stress, etc., the exiting light beams will have different phase relationships. If the two beams fall onto a white card, a disk with alternating bands of light and dark will be seen. Any intrinsic changes in one fiber, in comparison to the other, will be seen as a gradual shift in the light/dark pattern across the surface of the disk image.

Such an interferometer makes an ideal microenthalpimeter. Microdegree temperature changes can be detected. If an enzyme is immobilized on one arm of this interferometer, interaction with the substrate can be measured as a change in the phase angle relationship of the two beams. This can than be related to substrate concentration (Figure 10).[12]

The typical system uses a single detector. More advanced detectors use a linear array and some pattern-recognition technique identical with the way an eye follows pattern movement. A better way takes the sinusoidal intensity distribution seen by the linear array and performs a Fourier transform on the data. If x periods are displayed across the linear array, the ratio of the real and imaginary components of the xth spatial frequency in the inverse domain will lead to the phase angle required.

Unfortunately, most A/D subsystems cannot operate at speeds that match the maximum read-out rate of linear arrays. To use this detector system most effectively, a high-speed simultaneous (flash) converter with its own storage memory is needed. These are called transient recorders, since they were first used to trap transient signals. One-hundred-nanosecond conversion times are common. These devices usually transfer their information to the associated computer via a direct memory access (DMA) channel.

A more appropriate solution involves front-end electronic components that can manipulate the signal independently of

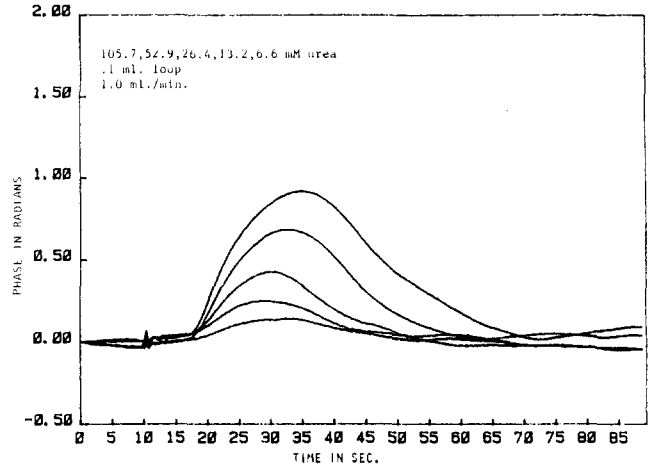

Figure 10. Typical enthalpimeter output from a Mach–Zehnder interferometer constructed from fiber optics. One arm has been coated with urease, and various concentrations of urea samples have been allowed to flow past the two arms of the interferometer. The phase shift in the recombined beams is plotted vs. time.

the computer. An analogy would be a logarithmic amplifier that converts transmission data to absorbance data before the computer digitizes it, obviating a time-consuming log conversion. Fourier-transform chips are available that can take an analog signal and convert it to its Fourier transform, producing a reduced data set.

Electrical engineers commonly use front-end electronic components. Many excellent modules are available from developments in the telecommunications industry. Laboratory scientists, still enthralled by the powers of digital programs running in their bench-top computers, have largely ignored these devices.

Spectral Decomposition via Correlation. A common problem in the laboratory is a spectrum derived from a sample with a number of components. Decomposition of IR spectra is an example. Many approaches have been described in the literature, most of them computationally intensive, particularly for a small microcomputer.

The matrices involved in linear parameter estimation are manipulated in a certain order to produce concentrations of the various components in a mixture. If the same matrices are manipulated in a slight different order, the approach is called correlation (Figure 11). The results are analytically the same. However, it is possible to purchase hardware modules that perform correlation in an analog domain. Like the Fourier-transform chips described above, they offer a front-end approach to spectral decomposition that avoids the intensive calculations required if a digital program is invoked. Studies on synthesized mixtures demonstrate that even nonoptimized hardware can decompose mixtures with five components satisfactorily.[13]

Engineering workstations and graphics terminals commonly use array processors and floating point processors to assist the main computer. Even personal computers are beginning to invoke math coprocessors to increase program throughput. Front-end electronics can do the same thing for the laboratory instrument.

SELF-OPTIMIZING INSTRUMENTS

All of the factors described comprise the skeleton and muscle of the laboratory instrument. What must be added are the elements of decision making that characterize the expert.

A variety of ways to explore the response surface for an analytical method have been published. These include Monte-Carlo methods, univariate analysis, the Simplex, and a variety of "designed-experiment" approaches. Smith Kline and French Laboratories have reported an elegant closed-loop

The observed absorbance spectrum of a mixture, A, containing three components, L, M, and N will be A_1 at wavelength 1, A_2 at wavelength 2, and A_3 at wavelength 3, for concentrations of the three components C_L, C_M, and C_N respectively.

$$(k_{L_1})(c_L) + (k_{M_1})(c_M) + (k_{N_1})(c_N) = A_1$$
$$(k_{L_2})(c_L) + (k_{M_2})(c_M) + (k_{N_2})(c_N) = A_2$$
$$(k_{L_3})(c_L) + (k_{M_3})(c_M) + (k_{N_3})(c_N) = A_3$$

In matrix notation:

$$\begin{bmatrix} k_{L_1} & k_{M_1} & k_{N_1} \\ k_{L_2} & k_{M_2} & k_{N_2} \\ k_{L_3} & k_{M_3} & k_{N_3} \end{bmatrix} = \underline{K} \quad \begin{bmatrix} c_L \\ c_M \\ c_N \end{bmatrix} = \underline{C} \quad \begin{bmatrix} A_1 \\ A_2 \\ A_3 \end{bmatrix} = \underline{A}$$

and

$$\underline{K}\,\underline{C} = \underline{A}$$

$$\begin{bmatrix} \Sigma\, k_{L_i} A_i \\ \Sigma\, k_{M_i} A_i \\ \Sigma\, k_{N_i} A_i \end{bmatrix} = \begin{bmatrix} CORR_{LA} \\ CORR_{MA} \\ CORR_{NA} \end{bmatrix} = \begin{bmatrix} k_{L_1} & k_{L_2} & k_{L_3} \\ k_{M_1} & k_{M_2} & k_{M_3} \\ k_{N_1} & k_{N_2} & k_{N_3} \end{bmatrix} \begin{bmatrix} A_1 \\ A_2 \\ A_3 \end{bmatrix}$$

or

$$\underline{CORR} = \underline{K}^T \underline{A}$$

The correlations of the reference spectra with the spectrum of a mixture need to be normalized for the autocorrelation of each of the reference spectra. The correlations of the references with a mixture must also be normalized for the differences in the cross-correlations of the references with each other. In matrix formulation:

$$\begin{bmatrix} \Sigma\, k_{L_i}^2 & \Sigma\, k_{M_i} k_{L_i} & \Sigma\, k_{N_i} k_{L_i} \\ \Sigma\, k_{L_i} k_{M_i} & \Sigma\, k_{M_i}^2 & \Sigma\, k_{N_i} k_{M_i} \\ \Sigma\, k_{L_i} k_{N_i} & \Sigma\, k_{M_i} k_{N_i} & \Sigma\, k_{N_i}^2 \end{bmatrix} = \underline{K}^T \underline{K}$$

$$(\underline{K}^T \underline{K})^{-1} \underline{K}^T \underline{A} = \underline{C}$$

In practice then, a measured spectrum $\underline{A}$ is correlated with a set of reference spectra $\underline{K}^T$ and the correlations are normalized to concentrations upon multiplication by $(\underline{K}^T \underline{K})^{-1}$.

Figure 11. Mathematical basis for spectral decomposition via hardware-correlation techniques.

implementation of a Simplex procedure for a self-optimizing organic synthesis. The batch reactor is computer controlled for the sequence of reagent additions and the ratios used. Temperature and stirring conditions are computer controlled. On the basis of initial experimental conditions input by the operator, the system is capable of exploring the response surface via a modified Simplex, locating an optimum procedure for the synthesis.[14]

Flow-injection analysis is an analytical tool that needs to be optimized and simultaneously provides the techniques necessary to do it. The pumps, sample loops, and temperature baths required are easily automated, along with the autosampler trays. Factorial-design and central composite design techniques can, with appropriate selection of an operating language such as FORTH, be placed in the small microcomputer responsible for the real-time control of the experimental conditions. FORTH is a language that has strong capabilities with respect to concurrency. Its terseness allows the complex programs involved to run at high speed in minimal memory.

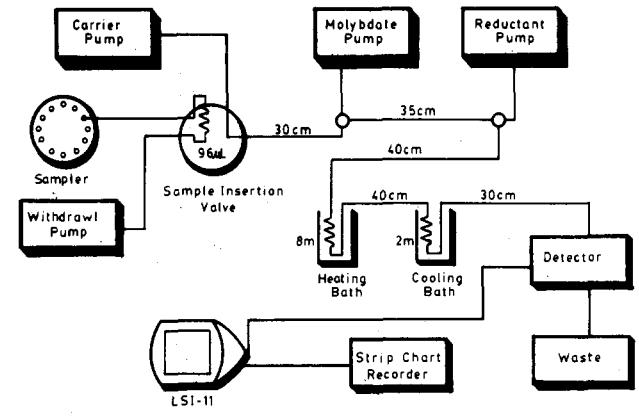

Figure 12. Self-optimizing flow injection analysis (FIA) apparatus.

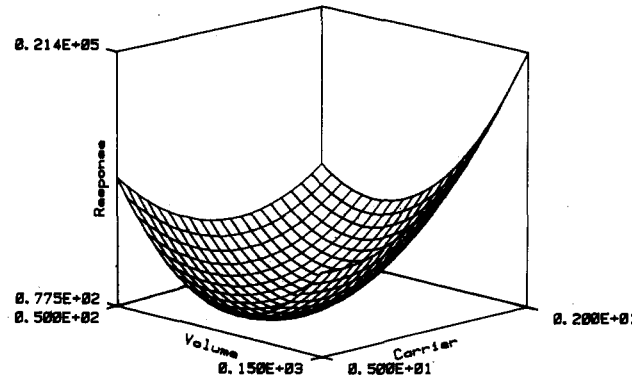

Figure 13. Typical 3-D plot from central composite design/factorial-design analysis of the response surface of an FIA determination of phosphate via the phosphomolybdate reaction.

With use of this approach, a methods development unit for self-optimization of FIA has been designed and tested (Figure 12). Once started, it runs unattended through the exploration of the response surface. At the conclusion, it reports the numeric and graphic findings to the operator (Figure 13).[15] The self-optimizing tool is a further step in providing intelligent instruments to the electronic laboratory.

The last step must wed artificial-intelligence concepts to these self-optimizing instruments. The reports of an expert system for X-ray fluorescence by Amoco,[16] neutron activation analysis by Schlumberger-Dole,[17] and GC/LC by Varian[18] clearly indicate the feasibility of this new dimension.

REFERENCES AND NOTES

(1) Wohltjen, H.; Dessy, R. E. *Anal. Chem.* **1979**, *51*, 1458–1475.
(2) Groetsch, J. A.; Dessy, R. E. *J. Appl. Polym. Sci.* **1981**, *28*, 161–178.
(3) Report to U.S. Air Force, 1978.
(4) Clifford, Paul "Chemical Sensors". *Anal. Chem. Symp. Ser.* **1984**, *17*, 153–158.
(5) Knipe, Charles R. "Particle Size Determination by Light Scattering and Hydrodynamic Chromatography". Dissertation, Virginia Polytechnic Institute and State University, 1983.
(6) Dessy, R. E.; Nunn, W. G.; Titus, C. A.; Reynolds, W. R. *J. Chromatogr. Sci.* **1976**, *14*, 195–200.
(7) Nunn, W. G.; Dessy, R. E.; Reynolds, W. R. "Multichannel Image Detectors in Chemistry". *ACS Symp. Ser.* **1979**, *102*, 135–167.
(8) Starling, Michael K. "An Automated Multicolumn Liquid Chromatography: A Feasibility Study in Full-loop Controlled Low Molecular Weight Separation Methods Development". Dissertation, Virginia Polytechnic Institute and State University, 1980.
(9) Binkley, D. P.; Dessy, R. E. *Anal. Chem.* **1980**, *52*, 1335–1344.
(10) Ishihara, F. personal communication.
(11) Lam, R. B.; Foulk, S. J.; Isenhour, T. L. *Anal. Chem.* **1981**, *53*, 1679–1684.
(12) Burgess, Lloyd W. "A Fiber Optic Interferometer for Enthalpimetric Sensing in a Flowing Stream". Dissertation, Virginia Polytechnic Institute and State University, 1984.

(13) Thompson, Mark R. "Evaluation of an Analog Front-End Processor". Dissertation, Virginia Polytechnic Institute and State University, 1983.
(14) Chodosh, Daniel F.; Levinson, Sidney H.; Weber, John L.; Kamholz, Kenneth; Berkoff, Charles E. *J. Autom. Chem.* **1983**, *5*, 103-107.
(15) Currie, James T. "A Response Surface Methodology Approach to Optimization in Flow Injection Analysis", Dissertation, Virginia Polytechnic Institute and State University, 1984.
(16) Ennis, Susan *Anal. Chem.* **1984**, *56*, 1326A-1332A.
(17) Barstow, David R. "Exploring a Domain Model in an Expert Spectral Analysis Program". "Sixth International Conference on Artificial Intelligence", Tokyo, Japan, August 1979.
(18) Karnicky, Joe *Anal. Chem.* **1984**, *56*, 1312A-1314A.

Laboratory Automation

JOSEPH G. LISCOUSKI
Digital Equipment Corporation, Marlboro, Massachusetts 10752

Received February 1, 1985

A number of factors are pushing modern chemistry laboratories to view laboratory automation as a necessity and not as a luxury. The cost of people, government regulations, and making the most effective use of human resources are just three of them. Understanding how we got where we are and the issues facing us are important to making real progress in this area.

INTRODUCTION

Today, the words "laboratory automation" almost immediately bring to mind computers and computer systems. That is a result of the current bias in our thinking and really does not reflect the true meaning of the words. The laboratory is a place to work, and automation refers to things being driven or guided by themselves. It really involves the work place, either all or part of it, functioning without our intervention or supervision. If we go back and reapply that meaning to the chemistry laboratory we will find that laboratory automation is not a recent—given the long perspective of chemistry—development but one that goes back over a couple of decades (some may argue that it dates to the invention of the graduate student, but I will restrict myself to mechanical or electronic means of automation).

Before we get too deeply involved in the topic of automation, let us take a quick look at the environment we are working in—at least those of us that work (or worked) in analytical labs. Our driving ambition is answering questions about samples: What is it? How much of a given component does it contain? Certainly not to be ignored are the problems of method development and the question "is it done yet?". Satisfying those questions involves determining the appropriate method of analysis, preparing the sample, performing the analysis, calculating the results, validating them, and finally preparing and sending the report to whoever submitted the sample in the first place. The goal of real laboratory automation is to reduce the manual effort in repetitive tasks as much as possible. Some day, when computer systems are smart enough, we may reach Lou Mikkelsens' (Hewlett-Packard, Avondale, PA) goal [1983 Pittsburgh Conference symposium: "Solving the Laboratory Data Management Problem" (unpublished)] of a system that will take the sample from bottle to finished result without our being involved at all, at least not for routine tasks.

The drive behind the automation efforts stems from two fronts: the laboratory chemist (predominately the human element) and his management (human element, efficiency, and economics). Both are faced with conflicting requirements: the need to perform more analyses (routine, nonroutine), to develop new testing techniques, and to do it within the facilities budget. The requirements of government regulations are added on top of that to keep things interesting. Manpower is an expensive, but required resource. The trick is to use people where they are most effective and some form of automation where it is effective. The right balance (easier to write than produce) benefits both management and the laboratory worker by reducing the need for people to do routine repetitive tasks and freeing them for more interesting work.

Joe Liscouski is currently a Marketing Consultant at Digital Equipment Corp. (Marlboro, MA). Prior to his 11 years at Digital, he worked for Dart Industries as an analytical chemist and product development chemist. He did his undergraduate work at Montclair State College in chemistry and his graduate work in computer science at Fairleigh-Dickenson University. He is the founding chairman for the Laboratory Automation Subdivision of the American Chemical Society's COMP division and has published over 14 articles in the areas of laboratory automation and data acquisition.

AUTOMATION BEGINNINGS

Automation in the chemistry laboratory began not with the advent of computer systems but most probably in the late 1950s for commercial systems, with the introduction of the Auto-Analyzer I (Technicon, Tarrytown, NY) and later the Auto-Analyzer II (1969-1970). These systems attacked the problem of automating the analysis. They would take the prepared sample, mix reagents, apply heating and mixing as required, and pass the sample through a photometric detector. The preparation and data reduction were still in the realm of human activities. There were some also systems developed on a one-at-a-time basis for automated work: there was an automated Karl-Fisher titration apparatus at Rexall Drug and Chemical (Paramus, NJ) in the mid 1960s. Automated process chromatographs were made by several companies.

0095-2338/85/1625-0288$01.50/0