LIMS Is Next Step in Laboratory Automation

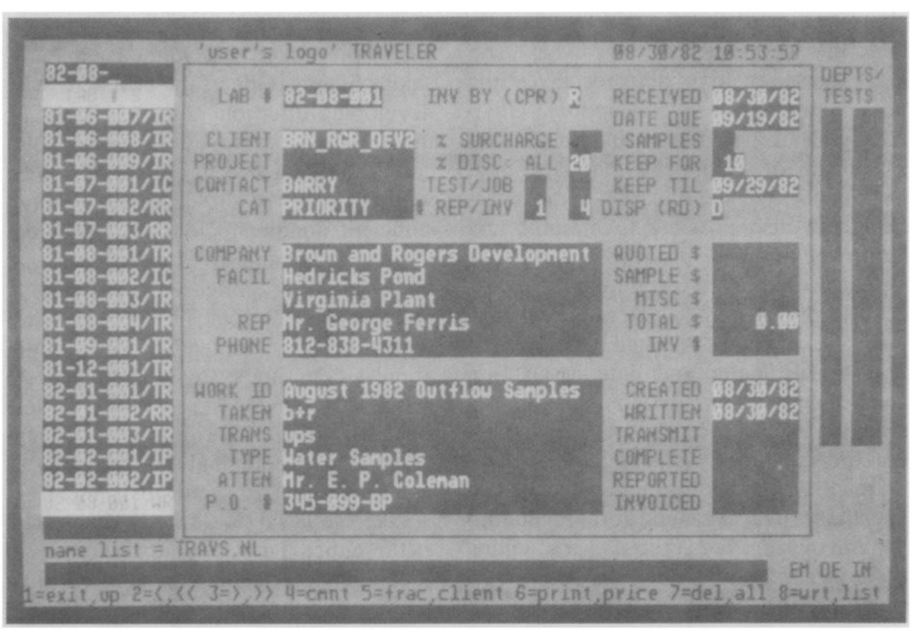
Computerized analytical instruments have the capability to spew forth torrents of data. Merely filling a laboratory with such machines will not, however, guarantee that they are used effectively to churn out the maximum number of chemical analysis reports in the minimum time for the least cost. The increasingly popular tool for accomplishing this task is the laboratory information management system or LIMS, which is a variant of the database management system concept that is widespread in the business world.

In one sense, a LIMS does not mean the same thing as laboratory automation. A LIMS-equipped laboratory is not a gigantic black box which accepts samples as input and produces reports as output. Still to come is the laboratory of the future portrayed by Louis Mikkelson of the Hewlett-Packard Company at a Pittsburgh Conference symposium entitled "Solving the Laboratory Management Problem," in which robots may play a major role or in which a liquid carrier system whisks samples identified by machine-readable labels from instrument to instrument. Similarly, LIMS systems do not automatically make important decisions such as ordering personnel to shift from one part of the laboratory to another or buying new equipment, although future computers endowed with artificial intelligence might do such things.

A LIMS shifts one's perspective from that of the analytical chemist concerned with the science and technology of analytical techniques to that of the laboratory manager who wants to run a cost-effective organization. Perhaps from the manager's point of view, but certainly from the LIMS point of view, the analytical laboratory becomes an information system with several sources of input data and several channels of output. The problem is to keep the system functioning smoothly. The often highly automated instruments so highly touted in previous Pittsburgh Conference reports become, in the words of Allen Lauer of Varian Associates, simply "transducers to put data into the system."

To see how a LIMS works, consider the coal analysis laboratory at the Department of Energy's Pittsburgh Energy Technology Center, as described by Gerst Gibbons to the laboratory management symposium. Gibbons said his goal was a paperless laboratory and that the laboratory was about two-thirds of the way toward achieving that end.

Samples of coal come into a receiving room, where they are logged into the system. Information collected includes the customer name, sample type, who is to get the analysis report, what analyses are to be done, and any special instructions. These data, along with a code assigned by the receiving room, go into the computer.



Radian Corporation

Sample tracking with a LIMS

Data entry into the Radian Corporation's SAM system is a matter of filling in the blank fields on a video display screen. There are standard forms for each of the LIMS tasks. Shown is a form whose completion initiates the sample tracking procedure. Many of the fields are filled automatically from information already in the data base.

A second class of input data is the collection of analytical results from the laboratory itself. This is a mixture of wet chemical data manually entered on a terminal and of data automatically acquired from computerized instruments, such as gas chromatographs.

The final category of input data is that entered by the laboratory supervisor. The supervisor must, for example, approve all results before they are released to the customer. He may instead order tests to be rerun, give special instructions to operators, or add his own comments to the report generated for the customer.

On the output side, Gibbons listed four types of reports. The first is that generated whenever there is sufficient data to do so. Such reports include receipts for customers when samples are submitted, analyses results to customers after the supervisor has given his approval, a schedule for each operator of samples awaiting analysis in order of their priority, and a status report for each sample that shows analyses that are pending, in progress, and completed.

Status reports are easily generated by the computer, in contrast to manual systems. Gibbons drew a laugh from the audience when he showed a slide of one old typed sample status sheet at the Pittsburgh laboratory that had been annotated in several different sets of handwriting. Locating a sample from this list was not trivial.

A second type of report is that composed daily. Such reports include lists of samples received and logged into the system that day, lists of samples completed and reported that day, and lists of any exceptional activities. The main example of the third category, weekly reports, is an accounting of man-hours worked by operators whose time is chargeable to reimbursable accounts. Finally, monthly reports list the analyses completed by each operator in each laboratory unit, the analyses requested of each laboratory unit, and the backlogged samples in each laboratory unit.

Among other things, laboratory supervisors can use this kind of information to look for logjams in the system. Perhaps too many requests for one kind of analysis are backing up the system and a new instrument is required. Or perhaps an operator is not performing efficiently and needs to be replaced. Or perhaps the scheduling of the types of analyses requested should be shifted.

Gibbons said that his laboratory handles about 20,000 coal samples per year with this system, which runs on a 16-bit minicomputer. How many samples would represent the economic break-even point above which a LIMS would pay for itself? At a press conference at the Pittsburgh Conference, Lewis Platt of Hewlett-Packard estimated that a laboratory receiving only a few hundred samples per year probably would not find a LIMS to be cost-effective, whereas one receiving a few thousand would. Platt noted, however, that computer hardware and software is getting less expensive in relation to manpower costs.

One might be inclined to praise these and other capabilities of a LIMS system and yet remain skeptical. The benefits of a LIMS are less tangible than those of, say, a minicomputer attached to a Fourier transform nuclear magnetic resonance spectrometer. The bottom line is to increase the productivity of the analytical laboratory, but exactly how a LIMS will do that is likely to be a little different in each laboratory and will require a lot of thought on the part of the purchaser.

With that word of warning, proceed to the wares shown on the floor of the Atlantic City convention center. Strictly speaking, LIMS refers only to software. But, one needs a minicomputer on which to run the software. Then there are terminals and other input/output devices. Finally, there are the instruments themselves that may have microcomputers or minicomputers associated with them. All the LIMS system shown at the Pittsburgh Conference are configured in a star network in which the minicomputer sits at the center with communications lines radiating to the associated nodes, which may be single "dumb" instruments with analog-to-digital converters, microcomputer-equipped "smart" instruments, or clusters of instruments grouped around a microcomputer or minicomputer.

Two manufacturers, the Perkin-Elmer Corporation and the Digital Equipment Corporation offered LIMS systems that run on 32-bit superminicomputers. These are very powerful machines that are capable of considerable "number crunching" and can directly address very large memories. Perkin-Elmer's system is called the LIMS/2000, was introduced at the Pittsburgh Conference 2 years ago, and has been installed in several laboratories. With Perkin-Elmer's 3230 supermini, disk drives, tape drives, terminals, software, servicing, and training, the system can cost from $80,000 to $400,000, with an average of $150,000 for systems sold so far, says Stephen Reber of Perkin-Elmer.

Digital Equipment introduced its LIMS/SM, although shipments will not begin until the end of the year. The SM stands for sample management and represents the first of four software groupings to be jointly developed with Varian. Digital does not make scientific instruments, and Varian does not manufacture computers, so the pairing plays on the strengths of each partner. Both companies will market the software, which is designed to run on Digital Equipment's VAX series 32-bit superminis. A Digital spokesman estimated $110,000 as the approximate price for LIMS/SM and other software, a small VAX (11/730), disk drive, console, and terminal.

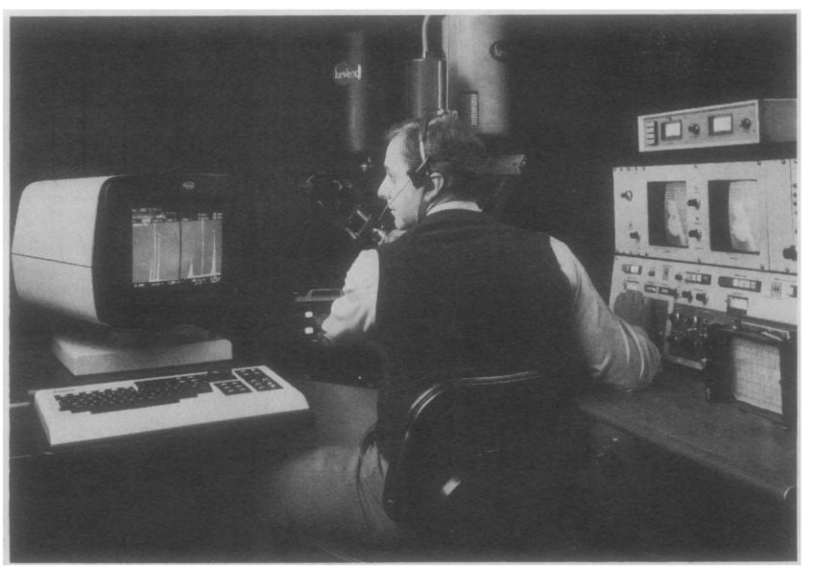
Three companies exhibited LIMS systems that run on 16-bit minicomputers, which are less powerful than the larger machines: Spectrogram Corporation, Radian Corporation, and Hewlett-Packard. The relative virtues of 32-bit and 16-bit minicomputers are probably best settled by the prospective purchaser. For the moment, for example, Spectrogram argues that a large network of instruments is more reliably served by two or three smaller minis than by one large machine because the other computers keep running, if one computer goes down.

Spectrogram's Labman system was introduced at the Pittsburgh Conference last year. A basic system consisting of a Digital Equipment PDP 11/23 minicomputer with two disk drives, a line printer, and video terminals is priced at $48,500. The largest Labman system sold so far involves a network of three PDP 11/23 Plus minicomputers and cost about $500,000.

Radian's Sample and Analysis Management (SAM) system was also introduced for the first time at the Pittsburgh Conference last year. The SAM runs on Data General Nova minicomputers. For $75,000, one gets the SAM software, the minicomputer, a disk drive, a line printer, and a console with video display and keyboard.

This year Hewlett-Packard is in the process of adding its LABSAM/3350 to its previously offered 3357 laboratory automation system, which runs on the company's HP 1000 series minicomputers. A company spokesman ventured that it would cost from $120,000 to $200,000 to equip a typical chromatography laboratory with this system, including operator training.

Three other companies exhibited laboratory information management systems that do not have full LIMS capabilities but do offer some related features: Bausch & Lomb, Inc., Mattson Instruments, Inc., and Rigaku/USA, Inc. Bausch & Lomb's Cast 11 is designed to accept data from the company's elemental analysis instruments and from those of the Leco Corporation. Mattson's Starlab is aimed at gathering data from Fourier transform nuclear magnetic resonance and Fourier-transform infrared instru-



The year of the gadget, part 2

Most analyses of scanning electron micrographs are performed in a dark room, where it may be difficult to see the microprocessor keyboard. The new Kevex Microanalyst 8000 is voice actuated so that the keyboard is bypassed. The instrument can be programmed to accept as many as 100 commands in any language. A recent test, the company says, showed that voice input was 17.5 percent faster than typing, and that typing produced 183 percent more errors.

ments from any of several manufacturers. Both Cast 11 and Starlab can merge data from different instruments into a report on a particular sample. Rigaku's MIS Software is tailored to run in conjunction with the company's x-ray fluorescence elemental analyzers.

Finally, Bolt Beranek and Newman Inc. exhibited an improved version of its RS/1 "electronic notebook." The RS/1 system stores data in two-dimensional arrays called tables. By means of English language commands, the user can display on a video screen in tabular or graphical form almost any relation between the data in any of these tables. To take a simple example, one table containing data arranged in several columns may be shown directly on the screen, after which the user commands a graphical representation of the functional dependence of one of the columns on another. A statistics package allows such things as curve fitting of the resulting graph. The electronic notebook has capabilities that overlap those of LIMS systems. Designed to run on Digital Equipment's PDP 11 series minicomputers and VAX superminicomputers, the RS/1 software will eventually be offered as part of the Digital Equipment/Varian LIMS system. Prices start at $13,500 for software to run on the smallest PDP 11 and go to $32,500 for the largest VAX.

In the future, star networks will likely be superseded by another form, the local area network, according to Joseph Liscouski of Digital Equipment and Melvin Marple of IBM Instruments, Inc. in separate talks at the laboratory management symposium. Rather than having a central computer with a cable to each node, local area networks consist of a number of nodes of essentially equal status arrayed linearly and connected by a single communications line. Another feature of local area networks is that resources located at one node are accessible to users at all nodes.

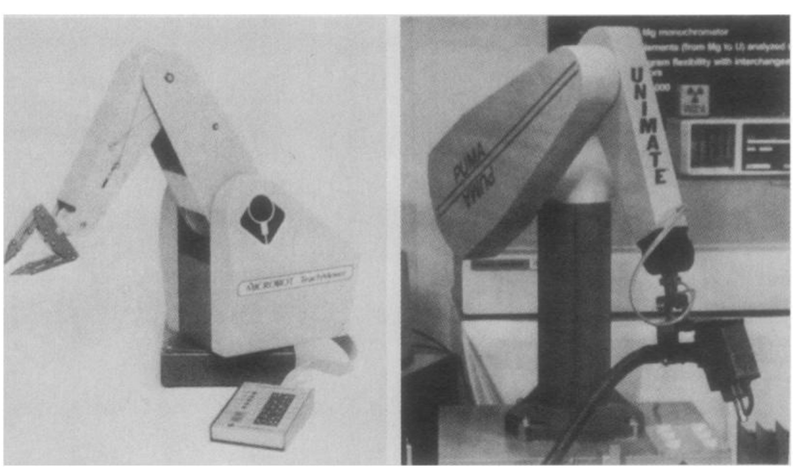
For the moment, they are expensive to implement and standards have yet to be fully worked out to allow different manufacturers' equipment to communicate, but local area networks are coming to the laboratory just as they are already appearing in office automation and similar situations. In his talk, Liscouski listed several reasons why, including high availability of the network resources to users at all nodes, rapid response to requests for resources from the users, resistance of the network to disruption due to failure of equipment at one node, ability of users at each node to control the equipment at their location, and the ability to handle high data rates.

In a local area network, a LIMS system would reside in a minicomputer at one of the nodes. One way to attach instruments to the network was described by Ira Gershenhorn of Purvis Systems, Inc. of Syosset, New York, in a Pittsburgh Conference talk. Purvis is building a local area network incorporating a LIMS for the Phillips Petroleum Company. The nodes of the network are work stations powered by 16-bit microcomputers based on the Intel Corporation 8086 microprocessor. Each node can handle up to 16 attached instruments. The network itself is the commercially available Ethernet, developed by the Xerox Corporation. Besides controlling its local instruments and accomplishing data reduction tasks, the work station can access other resources of the network, such as mass storage and input/output equipment, and it can serve as a terminal in the LIMS. In short, the work station functions as a local computer with certain capabilities and as a terminal of an effectively larger machine.

At the Pittsburgh Conference, two firms showed networking systems that did not have LIMS capabilities but nonetheless gave a little bit of the flavor of local area networks: Nelson Analytical, Inc. and Spectra-Physics, Inc. Nelson Analytical introduced its 5350 Sharesman resources manager, a software system that runs in conjunction with its 4400 series data systems for gas and liquid chromatography instruments. With the 5350 Sharesman, one could connect several data systems, each controlling several chromatographs, and one large-storage-capacity Winchester disk drive. The Winchester would be too expensive to add to a single data system, but the network capability allows it to be shared by all. The resources manager decides which data system can use the Winchester and when. Cost of a data system that can accommodate up to ten chromatographs is $13,200 and the networking software and disk drive are $9000.

Spectra-Physics showed its Labnet-equipped chromatography instruments for the second year. With Labnet, any instrument in the network can be addressed from any location, programs developed at one terminal can be transferred to any other, reports can be generated using data from more than one location, and so on. The Labnet capability is built into certain Spectra-Physics instruments, but a communications interface device priced at $17,500 permits other instruments or computers to be incorporated.

At the Pittsburgh Conference, five companies offered 16-bit microcomputers that were advertised as general purpose laboratory computers: IBM Instruments, Perkin-Elmer, Laboratory Technologies Corporation of Cambridge, Massachusetts, Digital Equipment, and Spectrogram. As Reber of Perkin-Elmer pointed out in his presentation to the laboratory management symposium, 16-bit minicomputers are rapidly being squeezed out between the declining price



The year of the gadget, part 3

Last year, the Zymark Corporation displayed a one-armed robot for automated sample preparation. This year, three new systems joined it. Microbot, Inc., of Mountain View, California, introduced two new systems (above left). One model is designed for educational use, while a more rugged version is designed for automation of laboratory tasks. A similar system was displayed by Yamato USA, Inc., of Northbrook, Illinois. A much larger one-armed system, the model 560 Unimate (above right), was displayed by Bausch & Lomb. This instrument is designed with the metals industry in mind, and can be used for on-site identification and sorting of metals and similar tasks.

of 32-bit superminis and the increasing power of the microcomputers. The 16-bit microcomputers have an important feature known as real-time, multitasking. This capability enables the computer to work on several jobs "simultaneously" and to respond to requests from instruments for data acquisition services immediately as needed. So, the makings of work stations in future local area networks are at hand.

For the record, IBM's 9000, which is based on a Motorola 68000 microprocessor, starts at $5700 but a usable system with disk drives and keyboard is about $8500. Perkin-Elmer's 7500, also based on the Motorola 68000, offers a color video display, and starts from $10,800. The Labtech 70 differs substantially from the other two microcomputers. It is built around Intel's 8088 microprocessor and 8087 coprocessor. The 8087 is an integrated circuit specially designed to make floating-point arithmetic operations very rapidly, and it gives the Labtech 70 a substantial number-crunching capability. The lowest priced version of the Labtech 70 is also a bit more expensive, starting at $13,800. Digital Equipment's new Labstation 23, which is a microcomputer version of the company's PDP 11/23 minicomputer, starts at $7695. At present, Labstation 23 is intended to link instrumentation to Digital Equipment's VAX superminicomputers. Finally, Spectrogram's Labmate V incorporates both a 16-bit (Intel 8088) and an 8-bit (Intel 8085) microprocessor so that older programs written for the smaller machines remain usable. Prices of the basic Labmate V start at $5900.

—**Arthur L. Robinson**

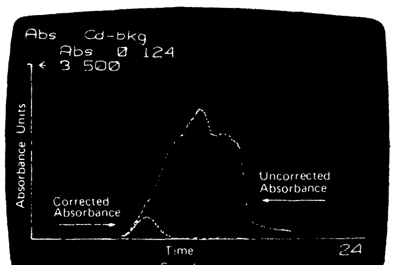
A New Way to Correct Background in AA

Correction for background absorption has always been a problem in atomic absorption (AA) spectroscopy. Because the conventional hollow cathode source emits light only at precise wavelengths, it is not possible to use it to scan the spectrum to provide background correction. It is thus necessary to use a second light source, typically a deuterium arc, to provide this scan. This dual lamp system, in turn, requires very precise alignment of the light sources and the use of a beam splitter, which reduces light throughput. The system also does not work as well in the visible region as it does in the ultraviolet.

One way around these problems is to use the Zeeman effect (*Science*, 7 Oct. 1977, p. 39). This involves enveloping either the furnace or the light source—but normally the furnace—in a strong magnetic field. When the furnace is in the field, atomic absorption occurs only in a polarization normal to the magnetic field, while absorption by the background occurs in polarizations both normal and perpendicular to the field. With an appropriate polarizing filter, it is then relatively easy to correct for the background. The primary drawback is that the magnet system is expensive, so that Zeeman effect spectrometers cost substantially more than conventional deuterium arc instruments. In certain cases, furthermore, calibration curves are double-valued, so that a given reading can represent two different concentrations.

A new and surprisingly easy way to correct background has been developed by Stanley B. Smith, director of research and development at Instrumentation Laboratory Inc. (IL), and Gary M. Hieftje of Indiana University. "We had been working together for a long time trying to find a better way to eliminate interference, but without a lot of luck," says Hieftje. "Then, one day 4 years ago, we were walking around Cambridge, England, after a spectroscopy colloquium when we both looked at each other and realized we had the answer." It has taken since then to work out the bugs and to incorporate the system into a commercial instrument, the IL Video 22.

The answer involved making use of a property of hollow cathode lamps that had previously been viewed as a liability. When a small amount of current is passed through a hollow cathode lamp, it excites an inert gas which, in turn, excites atoms of the element of interest, causing them to emit light at precise, narrow wavelengths. At higher currents, however, the emission lines are broadened significantly, which has the effect of reducing the sensitivity of the instrument. At still higher currents, nonexcited atoms of the source element are vaporized and absorb most or all of the light at the desired wavelengths; the net effect is that the source emits light at wavelengths other than those absorbed by the element of interest. This phenomenon is known as self-reversal, and was a condition to be avoided until Smith and Hieftje recognized that what the source was emitting was light that would be absorbed only by the background. "I look at what they have done," says a scientist from a competing company, "and I kick myself and say 'Why didn't I think of that?' "



Cadmium analysis

IL Video 22 AA screen during the determination of cadmium in 2 percent sodium chloride. Background absorption is 2.8 absorbance units (99.8 percent).

In operation, the Smith-Hieftje (pronounced Heef′-yah) background correction system operates by cycling the hollow cathode lamp through periods of low and high current. It is run at a low current for several milliseconds to determine the spectrum, then at high current for about 300 microseconds to measure the background. The actual times are precisely controlled so that the same number of photons reach the detector during each phase of the cycle. Recovery of the source when the current is reduced occurs in milliseconds. The electronics package then subtracts the background readings to produce the corrected spectrum. The system is particularly good, Smith says, for correcting structured background in which particles or unionized molecules in the sample chamber interfere with normal measurement of the analyte.

Because the Smith-Hieftje system is so simple, the new Video 22 is less expensive than a conventional deuterium arc spectrometer and significantly less expensive than a Zeeman effect instrument. The only important modification of the source that is required is additional insulation to prevent arcing when it is run at high currents. The company stresses that running at high current does not damage the source, and the sources are, in fact, guaranteed for the same amount of use as those in a conventional spectrometer. Because major changes in the electronics are required, however, it is not possible to retrofit the Smith-Hieftje system onto an existing AA spectrometer.—**Thomas H. Maugh II**