21 OCTOBER 1983 · VOL. 222 · NO. 4621

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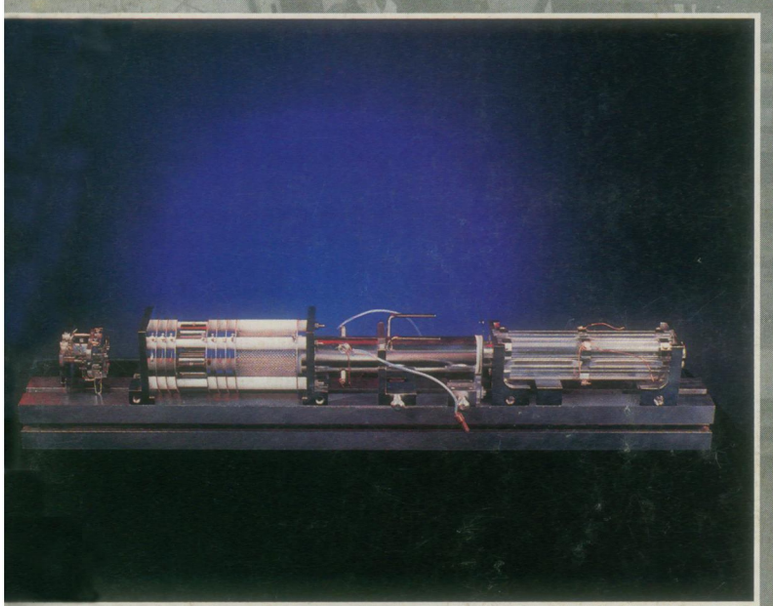

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The data system that goes beyond all others!

The new Beckman Model 450 Data System/Controller was worth waiting for. Designed expressly for chromatographers, this instrument goes beyond all others in providing what you want in chromatographic data acquisition, manipulation and storage.

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The Model 450 will gather, process and store data from as many as four HPLC or GC systems in your lab. But it's what you can do with that data that counts! On the large, clear CRT you can change baselines. Expand your chromatogram to examine a peak. Compare it to a stored standard.

And here's where Beckman leaves the others behind. If you team the Model 450 with our Model 165 Rapid Scanning UV/Vis HPLC Detector, you can calculate, plot and quantify absorbance ratios for peak identification and purity. That's a big help in spotting co-eluting peaks.

In fact, you can even perform on-screen spectral scanning. *No other system* has the hardware and software features to give you so much chromatographic information. And when you have exactly the data you want, the built-in printer/plotter gives you a completely documented hard copy of your results.

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And since the results are stored on disk, you can call them up for recalculation at any time.

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When you have a Model 450 actually installed in your lab, you'll find that the Beckman team also goes beyond all others in backing you up with ongoing applications, training and service. Start by calling your own Beckman sales representative now for complete details.

Or, to request a brochure on the Model 450, just phone TOLL FREE 800-556-1234 extension 503 in the continental U.S.; or 800-441-2345 extension 503 in California. The toll free lines are open from 5 a.m. to 6 p.m. PDT for product information requests only. In Canada call 1-800-268-2242. Or write Beckman Instruments, Inc., 1716 Fourth Street, Berkeley, CA 94710. (415) 527-5900.

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21 October 1983

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SCIENCE

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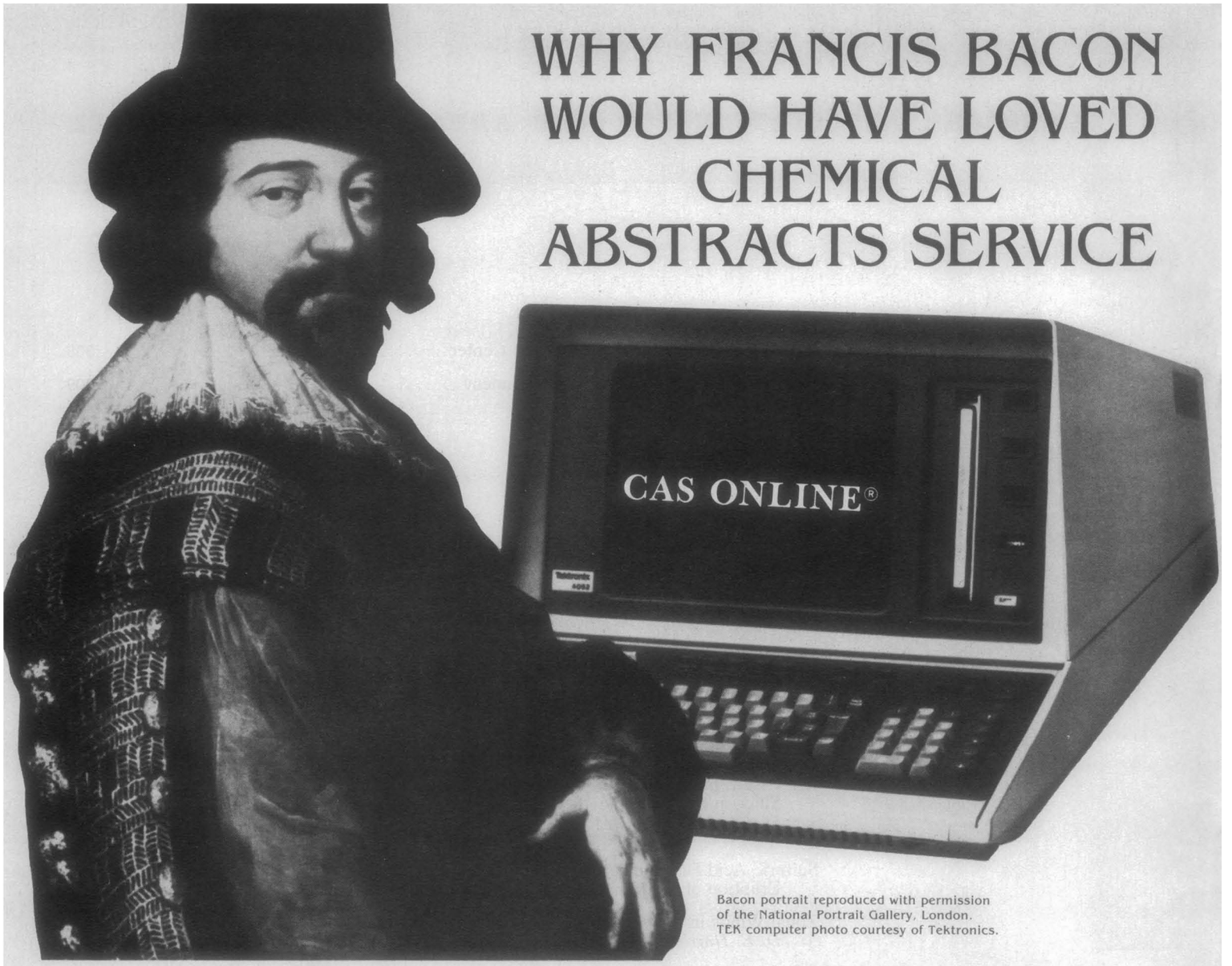
COVER

Large-scale mass spectrometers (background) used in preparation of isotopes at Oak Ridge National Laboratory. Essential elements (inset) of a tandem mass spectrometer developed for trace organic analysis in a joint academic/industrial venture between Purdue University and Finnigan Corporation. See page 273. [John Underwood, AV Productions, Purdue University, West Lafayette, Indiana 47907]

WHY FRANCIS BACON WOULD HAVE LOVED CHEMICAL ABSTRACTS SERVICE



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Even in Francis Bacon's time (1561-1626), there was too much literature to keep up with. He knew the solution was to be selective.

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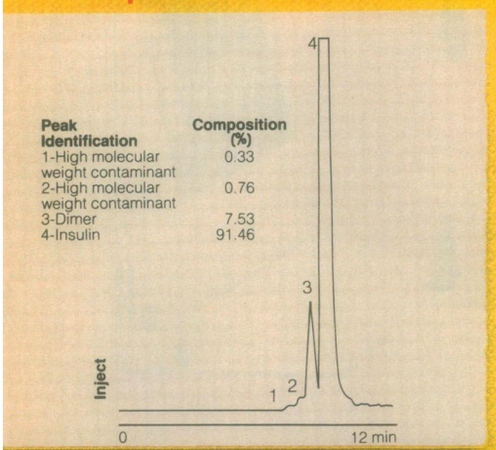
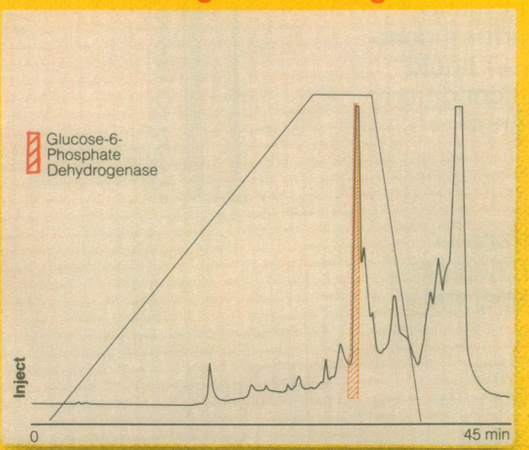


Separation time: 12 minutes.

Waters new high speed gel filtration methods allow rapid fractionation of protein samples. This same gel filtration method lets you profile sample composition, isolate all components and verify the purity of collected fractions.

Sample: 10 µl Insulin, 5 mg/ml
Column: PROTEIN-PAK 125
Eluent: 0.1% Trifluoroacetic Acid, pH 2.1
Flow Rate: 1.0 ml/min
Detection: 214 nm, 0.5 AUFS

Total recovery of enzymatic activity from a crude bacterial extract using ion exchange.

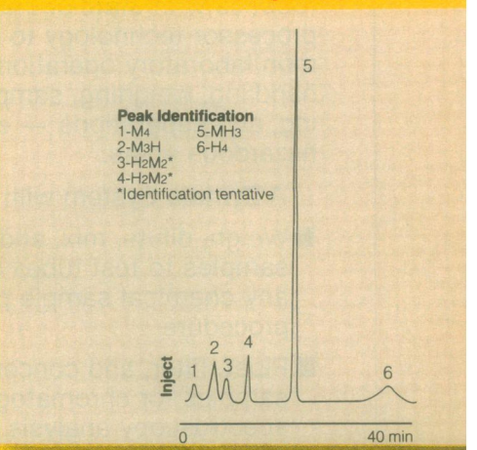


100% recovery of biologically active protein.

The large pore size of Waters polymeric ion exchange packings (1,000 Å) gives you recoveries of enzymatic activity approaching 100% for even high molecular weight enzymes.

Sample: 100 µl Bacterial Extract, 3 mg/ml
Activity: Glucose-6-Phosphate Dehydrogenase
Column: PROTEIN-PAK DEAE 5PW
Gradient Conditions
Eluent A: 0.02M Tris HCl, pH 8.5
Eluent B: 0.02M Tris HCl, pH 8.5 + 0.5M NaCl
0-100% B, curve 6, 25 min
Flow Rate: 0.5 ml/min
Detection: 280 nm, 0.1 AUFS
Specific Activity Increase: 4.9
Activity Recovery: 100%

High resolution ion exchange separation of isoenzymes.



Complete resolution of LDH isoenzymes.

The resolving power of Waters high performance ion exchange packings provides resolution of the closely related isoenzymes of lactate dehydrogenase.

Sample: 100 µl LDH Isoenzymes, 1 mg/ml
Column: PROTEIN-PAK DEAE 5PW
Gradient Conditions
Eluent A: 0.02M Tris Acetate, pH 8.0
Eluent B: 0.02M Tris Acetate, pH 8.0
+ 1.0M NaOAc
0-100% B, curve 6, 45 min
Flow Rate: 0.5 ml/min
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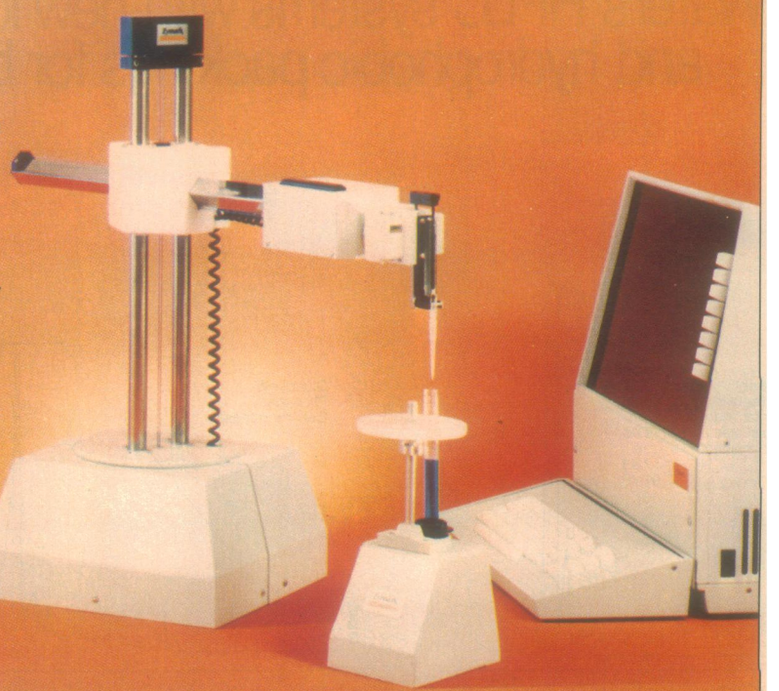

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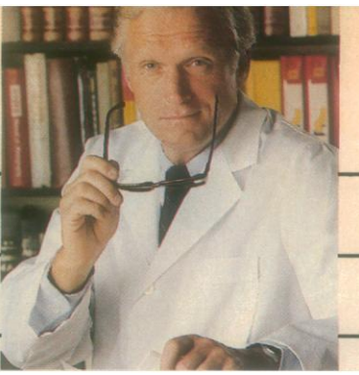
When wet chemistry can't.
When electrochemistry won't.



Dionex Ion Chromatography will!

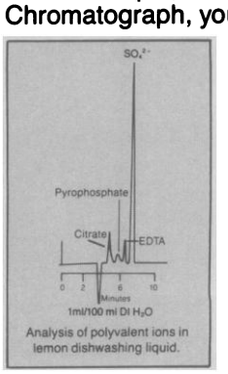
Many chemists are surprised to find out just how much Dionex Ion Chromatography can do—and how much time and money it can save!

If you think of Ion Chromatography in terms of simple inorganic anion and cation analysis, it's a little startling to discover that it can analyze organic acids and amines, sequestering agents, heavy and transition metals, amino acids and carbohydrates as well—in just about any sample matrix.

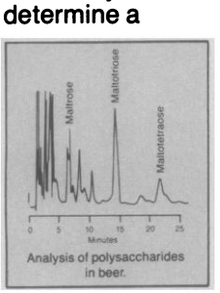
Watch a Dionex system in action

In many cases, a Dionex Ion Chromatograph is the only instrument you need to perform both complex and routine analysis on inorganic and organic anions and cations. And, thanks to the extraordinary selectivity of our advanced post column chemistries, usually all you have to do is "dilute and shoot."

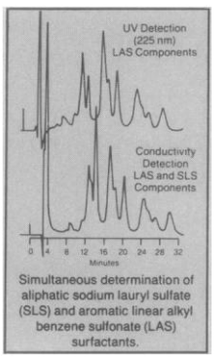
For example, with a Dionex Ion Chromatograph, you can detect ppm levels of polyphosphates, polyphosphonates, EDTA and other sequestering agents, even in brines in as little as 20 minutes. A Dionex system also lets you determine a complete range of alcohols and carbohydrates, including large polysaccharides—faster and more efficiently than any other technique.



Analysis of polyvalent ions in lemon dishwashing liquid.



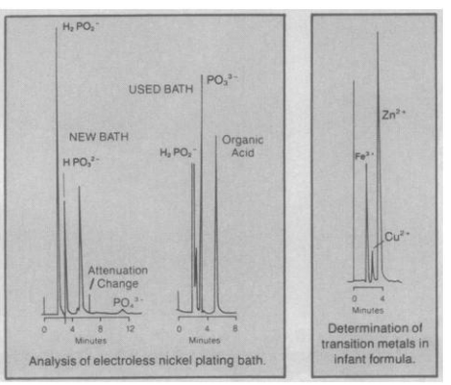
Analysis of polysaccharides in beer.



Simultaneous determination of aliphatic sodium lauryl sulfate (SLS) and aromatic linear alkyl benzene sulfonate (LAS) surfactants.

The same holds for organic acids and surfactants. Dionex column and detector technology makes Ion Chromatography a sensitive and specific alternative to GC and HPLC, whether the sample is oil recovery fluids, cosmetics, or detergents.

Of course, when it comes to inorganic ions and metals in samples such as chlor-alkali brines, plating baths, or even food, nothing—not even AA or wet chemistry—can compete with the sensitivity and convenience of a Dionex system.



Analysis of electroless nickel plating bath.

Determination of transition metals in infant formula.

Advanced technology only comes from experience

The key to Dionex versatility is proprietary column technology and superior detection based on advanced membrane post column chemistries.

Over the years, this technology has solved some of the toughest analysis problems in laboratories throughout the world.

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To give you the whole story, we'd have to fill this magazine with our application notes and details about our technical assistance program, training courses, and worldwide service network.

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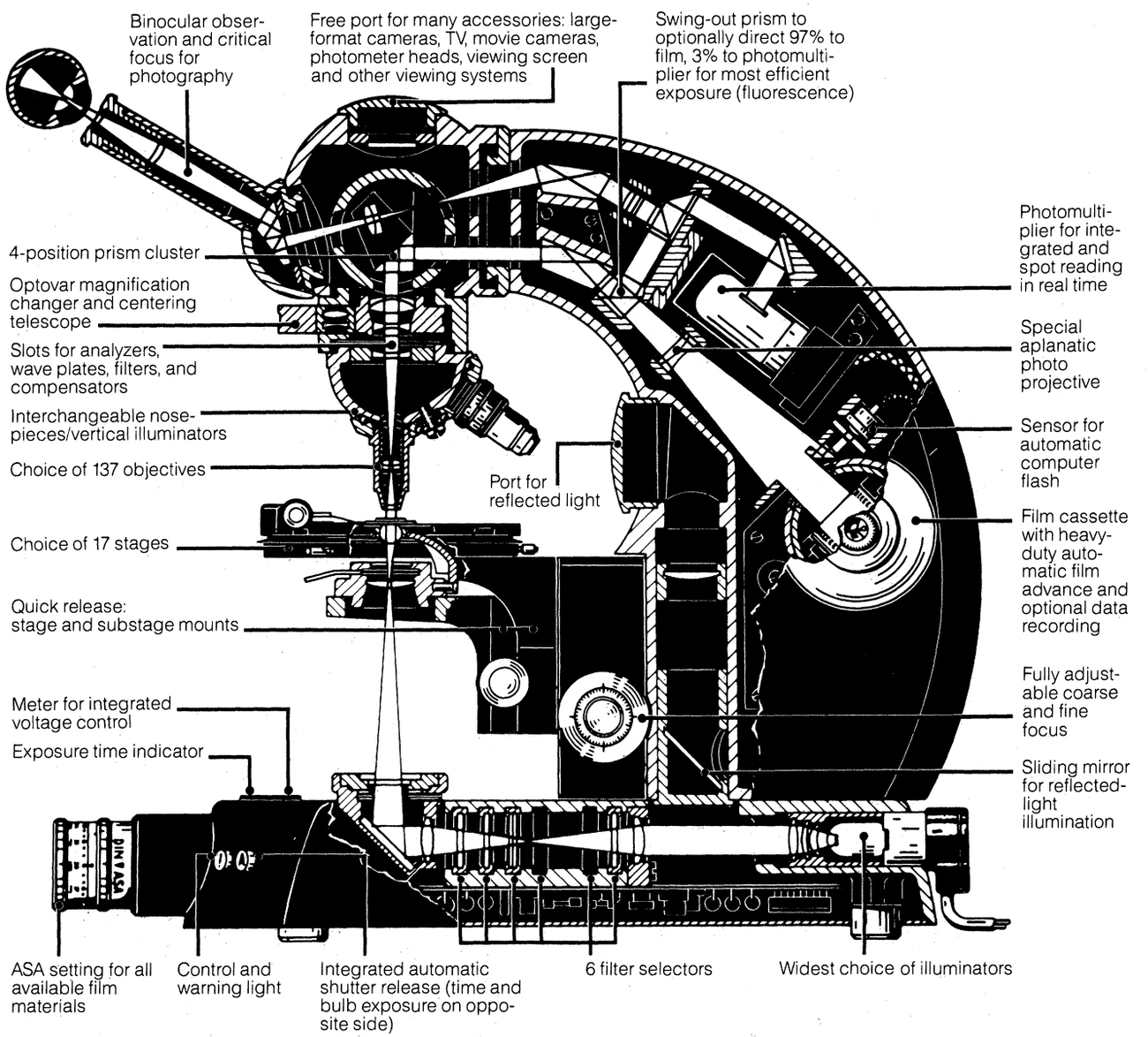

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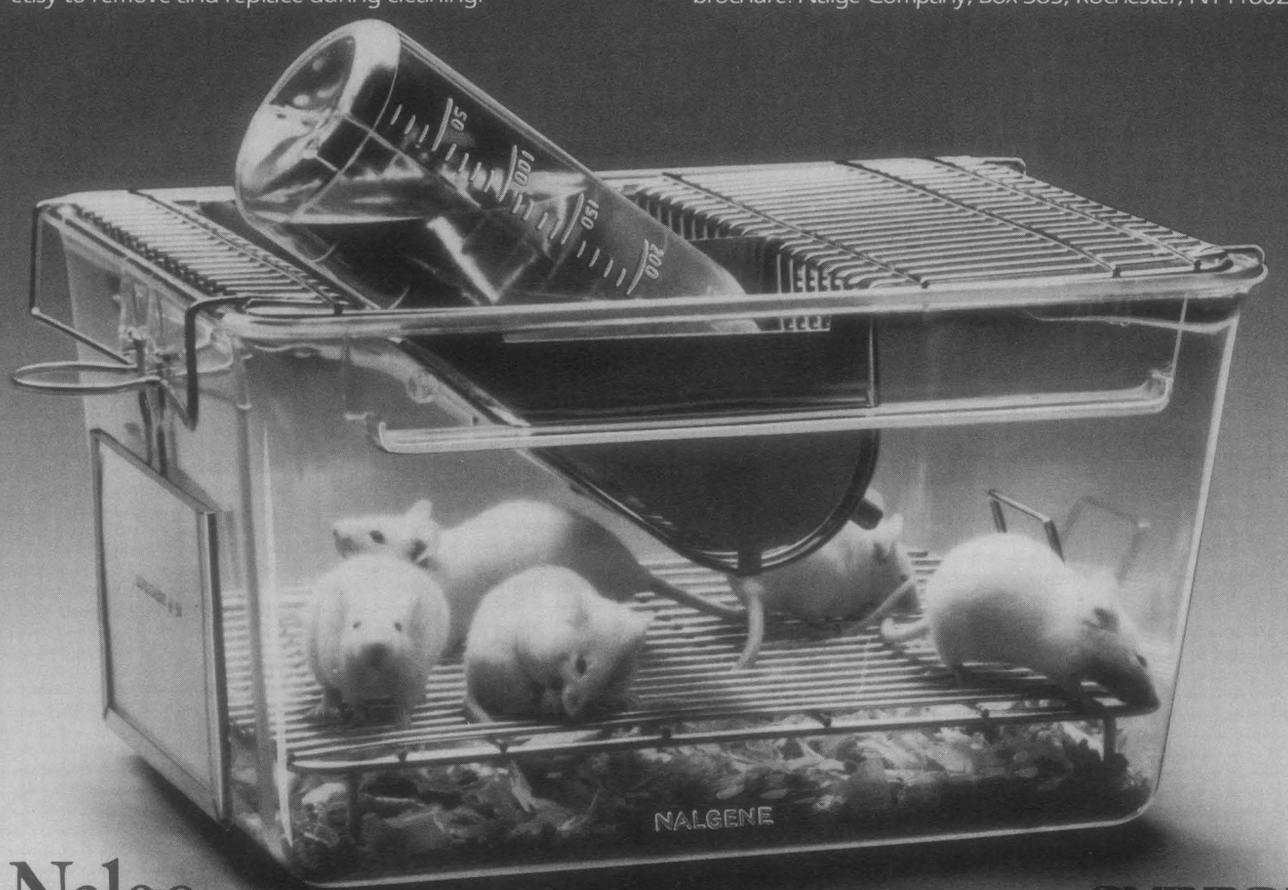

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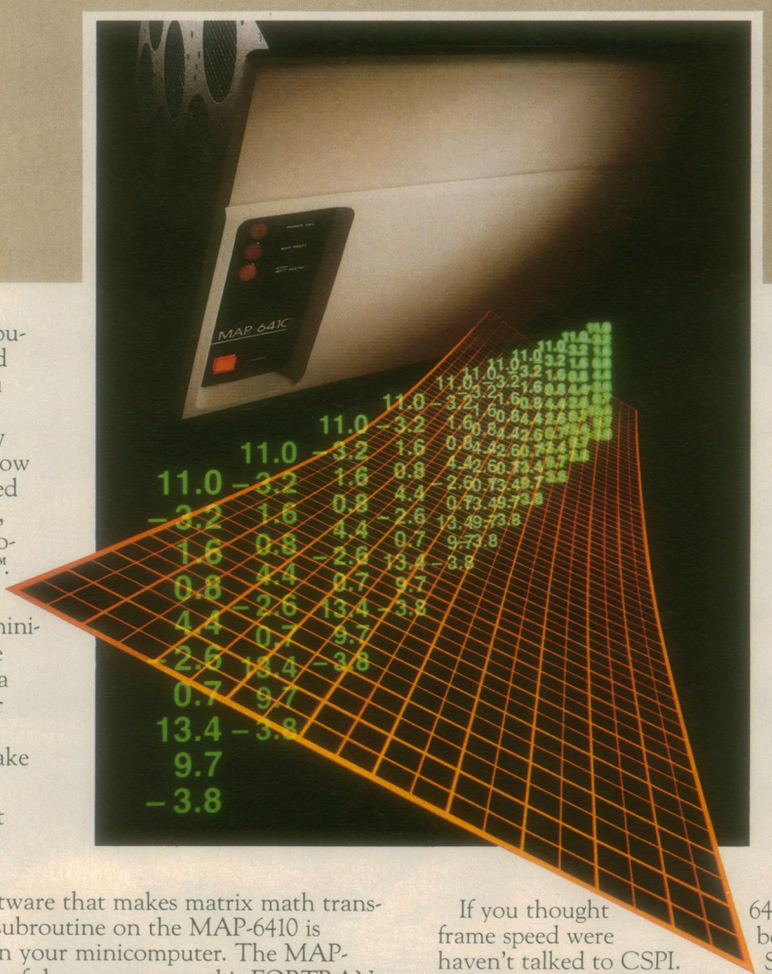

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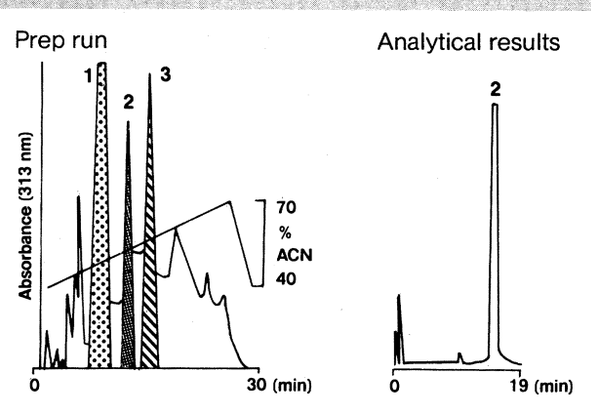
Isolate peptides and proteins with 99% purity

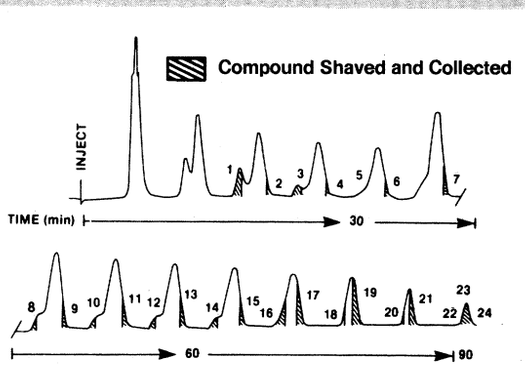


Problem: To isolate biologically active peptides and intermediate molecular weight proteins to 99% purity.

Solution: Isolate a crude synthetic peptide and protein extract to 99% purity without loss of biological activity by: performing a thirty-minute reverse phase gradient, collecting an enriched fraction of product, and rechromatographing a heavier load of the partially purified product under different gradient conditions.

Sample:	500 mg Peptide Hydrolysate
Cartridge:	PrepPAK® C_{18}, 57 mm x 30 cm (300Å pore, 30 μm particle)
Solvent:	A) 0.1% TFA in H_2O B) ACN: 0.1% TFA in H_2O, 40:60 0-100% B in 30 min, linear
Flow Rate:	150 ml/min
Detection:	UV, 313 nm

Purify natural product isomers with high yield



Problem: To purify three hard-to-resolve isomers with higher yield than traditional techniques.

Solution: By employing the exclusive shave/recycle feature of the PrepLC 500A System, the effective column length was increased to 26 feet (the sample was recycled 13 successive times without repetitive manual injection and collection) and a 77% yield of pure isomers was realized. This compares favorably to a 26.6% yield achieved with column chromatography.[1]

Sample:	.75 g Labdatriene Isomers
Cartridge:	PrepPAK® 500 Silica, 57 mm x 60 cm
Mobile Phase:	n-Hexane
Flow Rate:	250 ml/min
Detector:	RI

[1]*Journal of Liquid Chromatography* **4(3)** 525-532, (1981); *Journal of Organic Chemistry*, **46**, 3062, 1981

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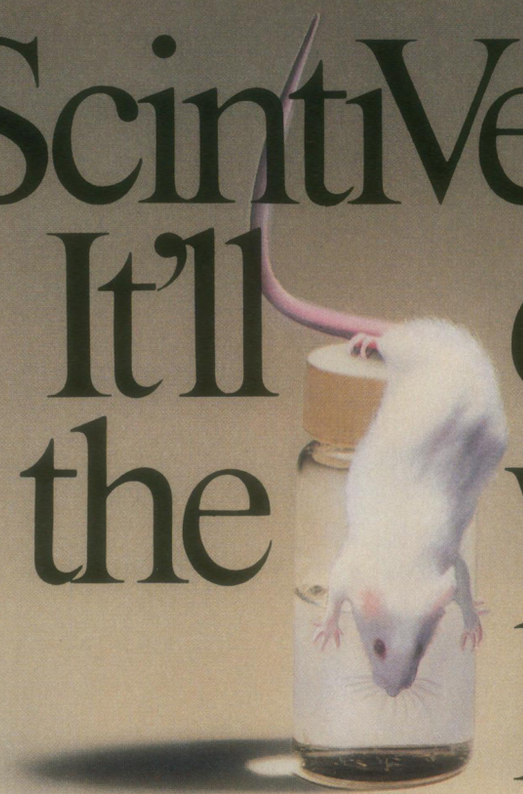

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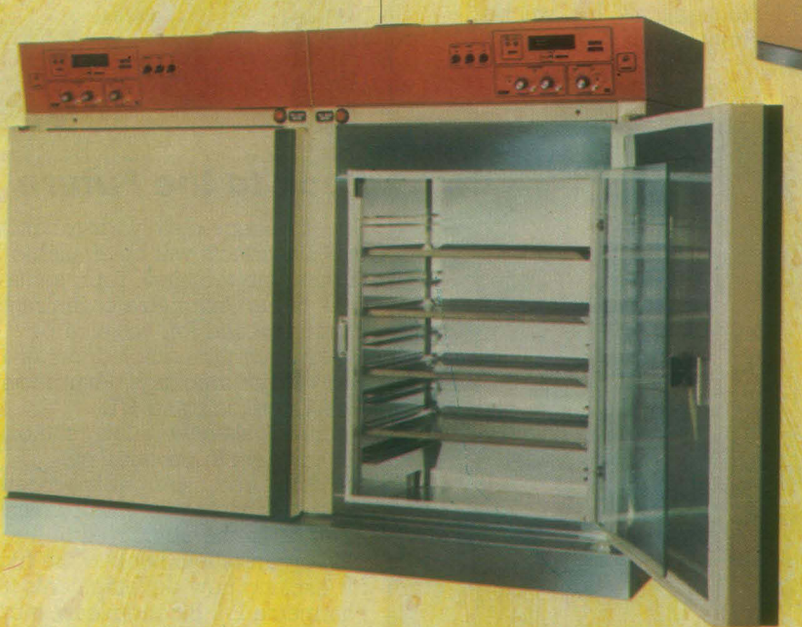

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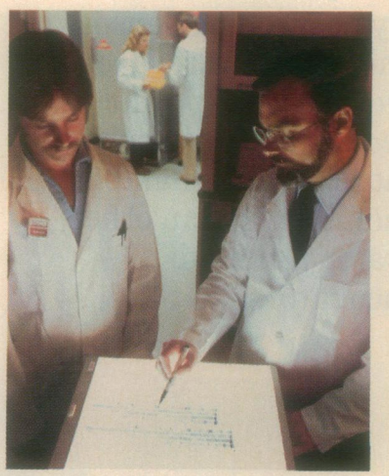

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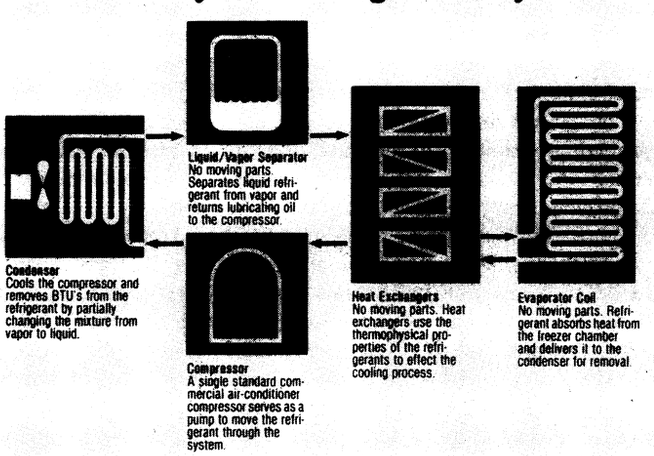

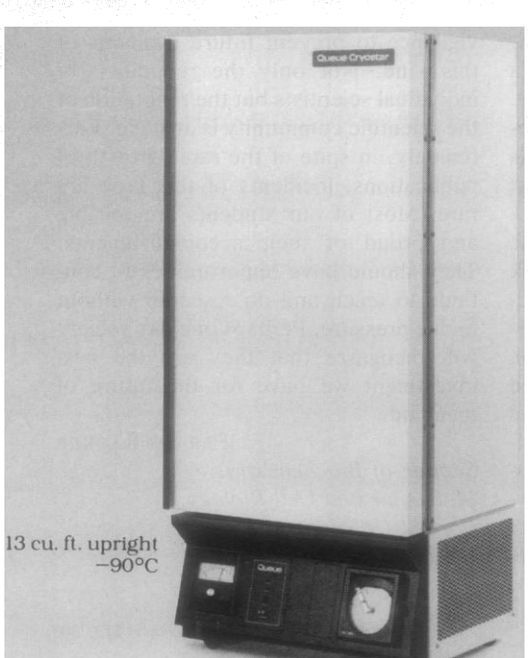

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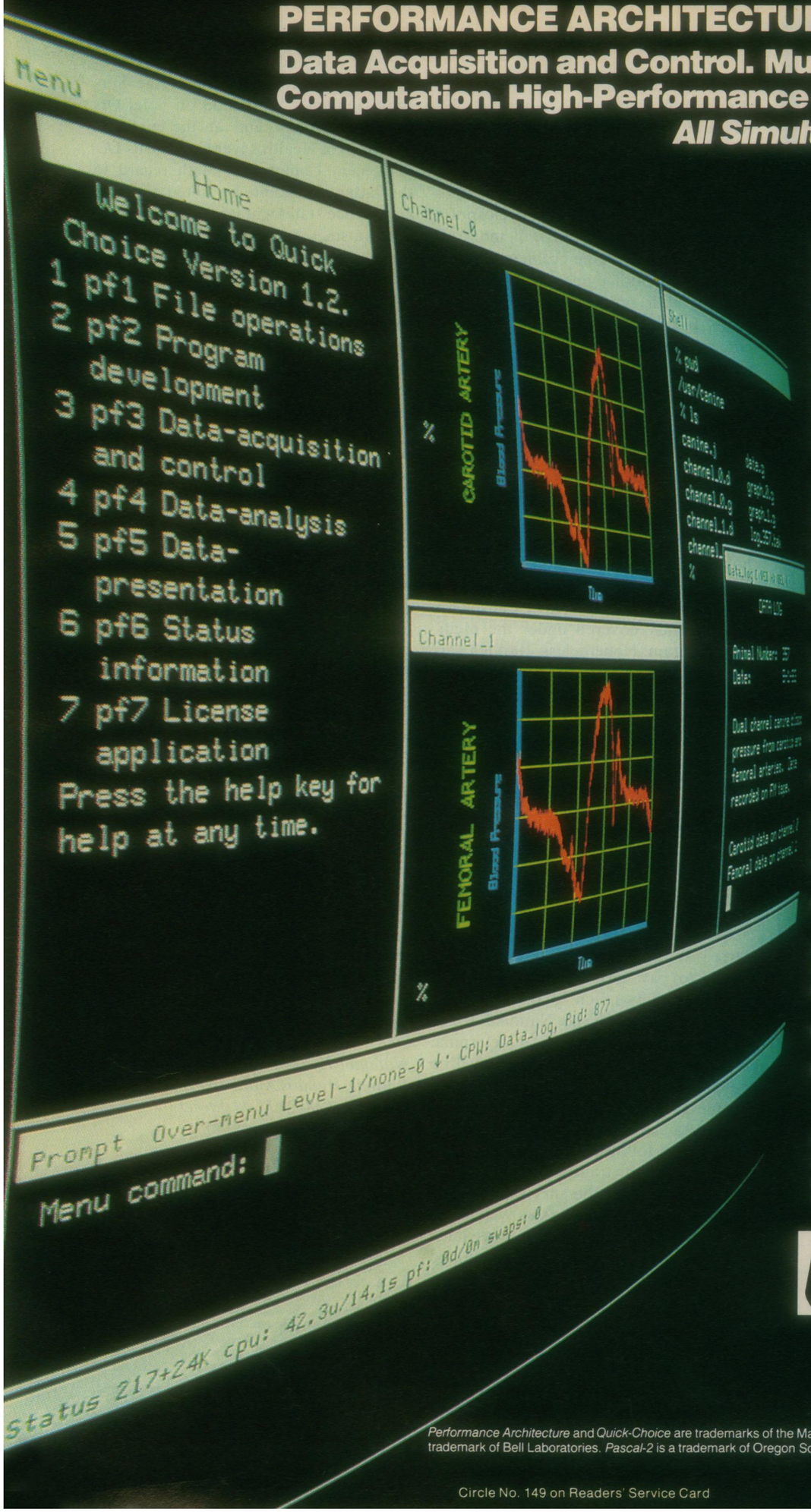

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Organ Transplantation

Several recent articles by Gina Kolata (News and Comment, 1 July, p. 32; Research News, 1 July, p. 40; 8 July, p. 139) suggest that we have now entered a new era in organ transplantation. While there are many reasons for this optimism, the availability of cyclosporin (Sandimmune) is foremost. It more effectively deals with the problem of rejection than traditional immunosuppressive therapy with prednisone and azathioprine. In addition, the rate of infection among transplant recipients has declined substantially with the use of cyclosporin. Unfortunately, the side effects of this drug, primarily nephrotoxicity and neoplasia, are not minor (*1*).

Despite the availability of cyclosporin, as Kolata points out, this new era of transplantation remains "clouded" because of the extreme shortage of donor organs. A further source of concern is how organ transplants will be paid for. Few private insurers routinely pay for transplants, and only kidney transplants are currently covered under the Medicare program. Nonetheless, through various circuitous means, the Medicaid programs of some states have paid for liver transplants.

The federal government has not, however, totally ignored the reimbursement or payment issue. The Health Care Financing Administration (HCFA) of the Department of Health and Human Services is currently sponsoring a major national study on heart transplantation (*2*). HCFA has responsibility for administering the Medicare program and consequently makes what are commonly referred to as coverage determinations (what to pay for) and reimbursement decisions (how much to pay) (*3*). The major objective of the National Heart Transplantation Study is to determine whether or not heart transplants will be paid for under the Medicare program. To enable HCFA to make this determination, data are being collected to address each of the following key points: (i) the need for heart transplantation in the United States; (ii) the survival rates for heart transplant recipients as well as for persons who fail to receive transplants because a suitable donor is not identified in time; (iii) the supply of viable donor hearts; (iv) the cost of performing heart transplants as well as the cost of providing medical care for patients who do not receive transplants; (v) the quality of life of heart transplant recipients; (vi) the legal issues surrounding heart transplantation; and (vii) the ethical issues associated with heart transplantation. In short, the study is addressing the key issues omitted from consideration at the Surgeon General's Workshop on Solid Organ Procurement and at the National Institutes of Health Liver Consensus Development Conference. With regard to the latter, it should be noted that the conference statement issued by the panel is but a single ingredient in the complex process of making coverage determinations. It does not bind private insurers nor the federal government to payment for liver transplantation.

Perhaps one of the less salient conclusions arrived at during the hearings before the House Committee on Science and Technology, the Surgeon General's Workshop, and the NIH Liver Consensus Development Conference was that organ transplant procedures cannot be assessed individually, nor can they be viewed apart from other pressing health care needs (*4*). Kidney, heart, liver, pancreas, bone marrow, and other organ and tissue transplants are likely to become more prevalent over the next decade. As a result, it appears that a national strategy is required to ensure the safety and efficacy of these procedures. It is equally apparent that transplantation represents only one technology in the complex armamentarium of health care technology. Consequently, the future development and growth of all health care technologies must be subjected to careful scrutiny to ensure that they are cost-effective. Technology is not without its price, and society must be prepared to decide the price it is willing to pay for health care. Neither individuals nor society can ignore the cost associated with providing the finest health care obtainable. Some very difficult issues are yet to be confronted, and equally difficult choices remain to be made.

ROGER W. EVANS
National Heart Transplantation Study, Battelle Human Affairs Research Centers, 4000 N.E. 41 Street, Seattle, Washington 98105

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1. *Lancet* **1983-I**, 1083 (1983); P. J. Morris, *Transplantation* **32**, 349 (1981); I. Penn, *Cancer Surv.* **1**, 621 (1982).
2. R. W. Evans, A. Anderson, B. Perry, *Heart Transplant.* **2**, 85 (1982); H. Newman, *Fed. Regist.* **46**, 7072 (1981); R. A. Knox, *Science* **209**, 570 (1980); R. W. Evans, *Heart Transplant.* **1**, 243 (1982).
3. L. D. Schaeffer, in *Critical Issues in Medical Technology*, B. J. McNeil and E. G. Cravalho, Eds. (Auburn House, Boston, 1982), p. 151.
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Erratum: In the report "Pregnancy interception with a combination of prostaglandins: Studies in monkeys: by J. W. Wilks (30 Sept., p. 1407), figures 2 and 3 on page 1408 were interchanged.

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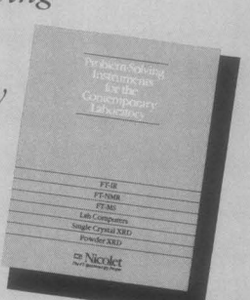

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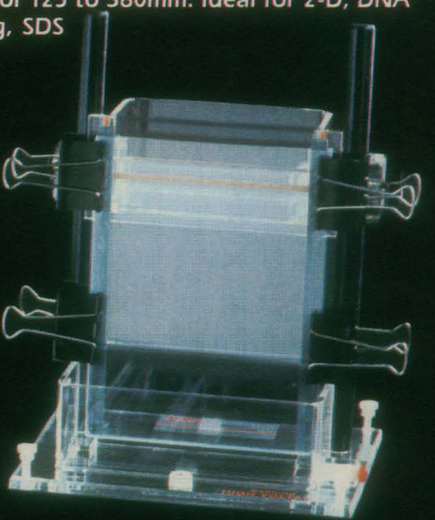

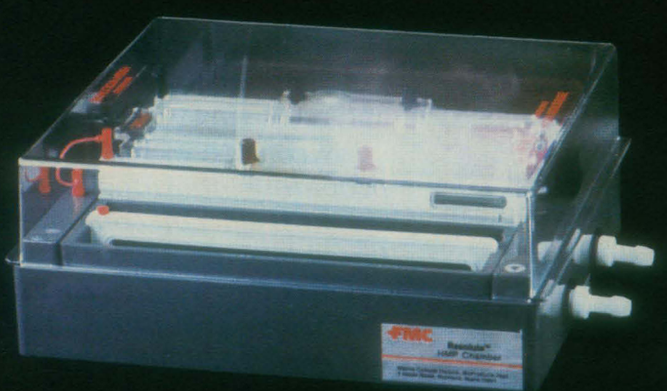

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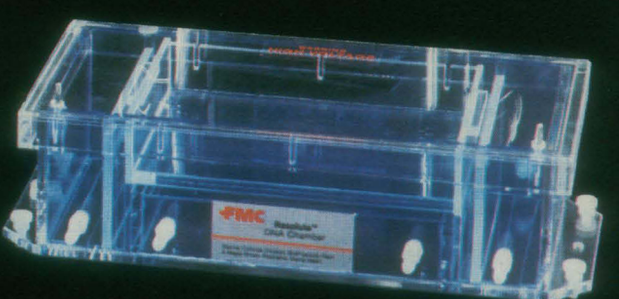

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BIOSYSTEMS UPDATE

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Phycobiliproteins possess their unique properties because they contain multiple bilin chromophores (as many as 40 in phycoerythrin) covalently bound inside the intact protein and thus significantly isolated from the protein's external environment. As a result, they display the following impressive properties:

- extinction coefficients $>2 \times 10^6 cm^{-1}M^{-1}$
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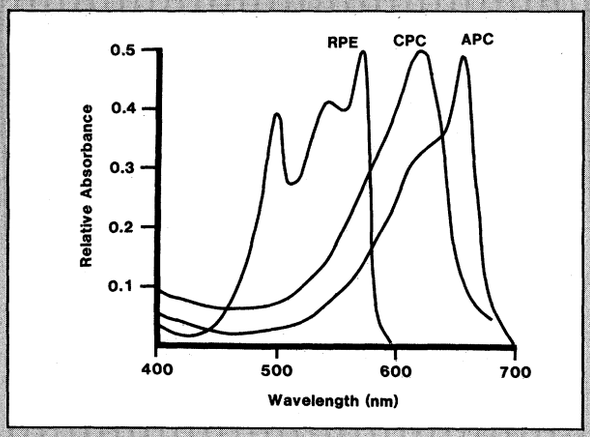
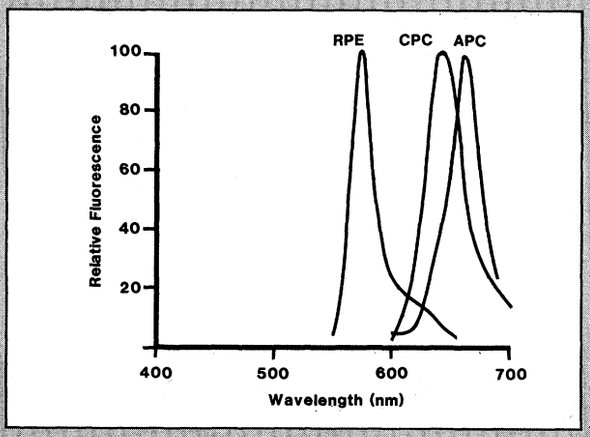
- wide spectral coverage—especially at the red end of the spectrum where natural interferences are minimal
- large Stokes shifts
- constant quantum yield over a broad pH range
- immunity from collisional quenching





Because phycobiliproteins are stable and highly water soluble, they can be easily linked to molecules such as antibodies with a variety of common protein cross-linking reagents.[1] The resulting conjugates are stable and offer significant advantages over conventionally tagged reagents. Recent research has demonstrated the usefulness of such conjugates in two-color fluorescent labeling of cells and in fluorescence immunoassay.[1,2]

Applied Biosystems is now making highly purified phycobiliproteins available to the research community for fluorescent labeling applications.

These phycobiliproteins are sold for research use only. Patents are pending.

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11 Questions to ask before you buy an automated DNA synthesizer.

1 Do I really need an automated DNA synthesizer?

The answer depends on your requirements for custom oligonucleotides. If you need more than one oligomer per month, an automated DNA synthesizer will be a good investment. However, if you use less than one per month, you should consider ordering custom oligomers or synthesizing them manually.

2 What advantages will an automated synthesizer provide?

An automated DNA synthesizer will perform all of the time-consuming procedures necessary to synthesize an oligomer—without the error potential inherent in manual methods. You'll be able to synthesize more product in far less time, and you'll be freed to dedicate your energies to other important tasks.

Another advantage is around-the-clock synthesis operations. If you select a quality synthesizer—such as the Coder™ 280—you'll be able to run syntheses 24 hours a day. That can further enhance your productivity.

3 How much does an automated DNA synthesizer cost?

The purchase price of an automated DNA synthesizer will range from about $21,000 to $68,000.

But you should consider the reliability of the equipment and the manufacturer's dedication to service. Downtime or long waits for service can impede your productivity, costing you valuable time and expensive chemicals.

4 What are the differences among the DNA synthesizers currently available?

Every synthesizer on the market today does basically the same thing. The primary differences are in the modes of fluid movement (pump or pressure driven), the type of reaction chamber (flow-through column or agitated vessel), and the number of reagent reservoirs. All types have been proven effective.

Nevertheless, in evaluating synthesizers, be sure to consider the reputation of the manufacturer and the experience of the company's scientific personnel.

5 Will a synthesizer do all the work?

All synthesizers will do the work involved in the synthesis itself, and some systems also will cleave your product from the resin. However, your product will be in crude form at this point, requiring purification by HPLC, electrophoresis, or other methods.

6 What kind of results will an automated DNA synthesizer produce?

You can expect results equal to those produced by manual synthesis techniques. Yields will average around 95% per base coupling, provided that you use high-quality reagents and take care in handling these materials. But even the best reagents handled with the utmost care will occasionally generate yields lower than 95%, regardless of some manufacturers' claims.

7 Which chemistry is best?

There are basically two types of solid-phase chemistry being used: phosphate-triester and phosphite-triester. Each has its advantages and disadvantages, depending on the specific requirements of your synthesis operations, and each has been proven to produce quality results.

The best choice is a synthesizer that can perform all solid-phase chemistries, rather than a system that is limited to only one method.

8 How much will it cost to run a synthesizer?

Exact figures are difficult to project, given the wide range of costs for chemicals and other factors. However, you should be able to produce 5 O.D. units of a purified pentadecamer for less than $125 for all reagents and solvents.

9 What problems should I anticipate with an automated synthesizer?

Even the best laboratory equipment will experience some downtime, and lesser quality synthesizers may break down or malfunction frequently, especially if they are being used continuously.

As a consequence, you should choose a manufacturer who has a qualified, responsive field service department—one that can provide both on-site and over-the-phone technical assistance and support.

10 Can the synthesizer's microcomputer be used for other duties?

If the synthesizer has a stand-alone microcomputer as a controller, such as the Coder 280 with Apple //e™ the answer is yes. The controller can then provide your lab with additional computer capabilities such as statistical analysis, word processing, and other lab management functions.

11 Will an automated DNA synthesizer do peptide synthesis as well?

If your synthesizer is user programmable, it is possible to do solid-phase peptide chemistry. However, it is not very practical because peptide syntheses usually require a minimum of 1 g. of resin and DNA synthesizers are designed to accommodate not more than 200 mg. of resin.

Furthermore, most DNA synthesizers are not designed to handle corrosive reagents such as trifluoroacetic acid. Versatile peptide synthesizers are.

Vega Biotechnologies wants you to be fully informed about automated DNA synthesizers—before you make your decision.

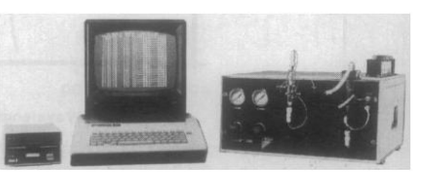
We invented the automated DNA synthesizer, and we offer the widest range of systems—including our Coder 280 with Apple //e microcomputer.

If you're in the process of evaluating synthesizers, or if you've simply been thinking about automating your DNA syntheses, call us toll-free at 800-528-4882. We'll send you more detailed information on our DNA synthesizers, answer any other questions you might have, and arrange a free demonstration.

The bottom line is this: Make sure you understand everything about automated DNA synthesizers before you invest in a system.

Vega Biotechnologies can help.

Call us, today.



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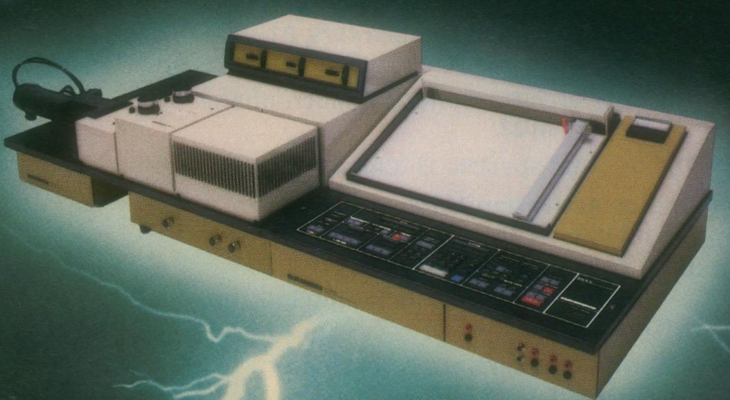

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21 October 1983, Volume 222, Number 4621 **SCIENCE**

Competition in the International Marketplace

Americans must face the reality that strong international competition is here to stay. During the past several decades, the world industrial competitive order has undergone major transformation. Multinational corporations grew in importance. The European Common Market and Japan became major economic and competitive forces, and the Soviet Union consolidated its influence in substantial areas of the world. Meanwhile, newly industrialized and resource-rich nations emerged as competitors. After the oil crisis of 1973–1974, the industrial world's economic growth slowed as inflation surged. Finally, in many nations, government-managed social services grew rapidly, often at the expense of the private sector.

These changes have coalesced to create a dynamic global competitive environment of which the United States is, of necessity, a part. On a constant dollar basis, our exports have more than tripled since 1960, and imports have risen almost as rapidly. Yet our competitive margin in some industries has either disappeared or is shrinking.

In contemplating these problems, it is fashionable and often instructive to examine the elements of success in certain Japanese industries, but it is more directly helpful to look at successful industries here at home. Our computer and telecommunications industries remain in the vanguard. We lead in aerospace technology, with all that this means in many fields, including national defense. Our petroleum industry has remained the world's pacesetter in technology for finding and winning oil and gas. Progress in these and other industries is buttressed by exceptional science and engineering capabilities in the universities and industry, as well as by high competence in the construction and engineering crafts.

The chemical industry, which I know best, is a strong international competitor. Chemical production in this country has grown at almost twice the rate of total U.S. industrial output. Nearly 40 percent of world chemical sales are generated by American-owned companies. Five of the 17 leading U.S. exporters are chemical firms, and the industry's shipments abroad yielded an $11 billion trade surplus in 1981. This competitive vitality has many sources. U.S. chemical companies have had a favorable raw material and energy base as well as a large domestic market. But chemical industry management has also paid attention to other elements:

- Research and development have been supported by top management, and the commitments important to a high rate of technological advance have been made. The industry accounts for 10 percent of all research expenditures in the United States, or close to twice its share relative to GNP.
- The industry has never viewed its opportunities as limited. It has steadily broadened its base by developing evolutionary product lines.
- Diversification into new, yet related, businesses and technologies, such as electronics and other high-technology areas, has been common.
- Productivity improvement and cost reduction have been pushed vigorously. Conservation programs have cut the industry's energy consumption per unit of output by 25 percent since 1972. Physical production per man-hour is twice the average level for total U.S. manufacturing.
- Investment in new plant and equipment has averaged between 6 and 8 percent of sales since 1970. This is roughly a third higher than the investment rate for the total manufacturing industry.
- Finally, the chemical industry has worked hard both to build exports and to establish plants and offices overseas. This two-track approach strengthens both domestic and international operations.

Most of these principles can be applied to other industries. The United States has the talent and resources and the toughness of mind to compete in the international marketplace. We must put our objectives in clearer focus and muster the will for their achievement.—EDWARD G. JEFFERSON, *Chairman of the Board, E. I. du Pont de Nemours & Company, Wilmington, Delaware 19898*

Based on an address presented at the Forum Club of Houston, Houston, Texas, 17 March 1982.

When you want constant temperature, how do you get it?

New Lauda digital circulators from −120° to +350°C with convenient LED display and unique safety control.

The smart way to get constant temperature is with one of 28 new circulators from Lauda, systems that keep hot things hot and cold things cold with dependable accuracy and precision.

A newly designed digital temperature setting gives you control accuracy to ±0.01°C and a digital readout displays actual temperatures in easy-to-read LED numerals.

Lauda advances also include a proportionally integrated differential control, which adjusts heater wattage according to heat load and automatically compensates for set-point drift.

And two models feature a built-in microprocessor-based programmer, which further assures accuracy and precision with a number of predetermined functions.

Lauda controls temperatures in other ways, too. For example, unique safety features like variable over-temperature controls and low-liquid-level indicators interrupt power should a problem occur. Zero crossover switching/RFI suppression eliminates the possibility of electrical interference with other instruments in the lab. And built-in flow control varies the rate of external circulation.

Dependable accuracy and precision are just part of the benefits of being Lauda. To learn more about the others, contact your Brinkmann representative; or call or write Brinkmann Instruments Co., Division of Sybron Corporation, Cantiague Road, Westbury, NY 11590, Tel: 800-645-3050; in New York, 516-334-7500. In Canada: 50 Galaxy Blvd., Rexdale, Ont. M9W 4Y5, Tel: 416-675-7911.

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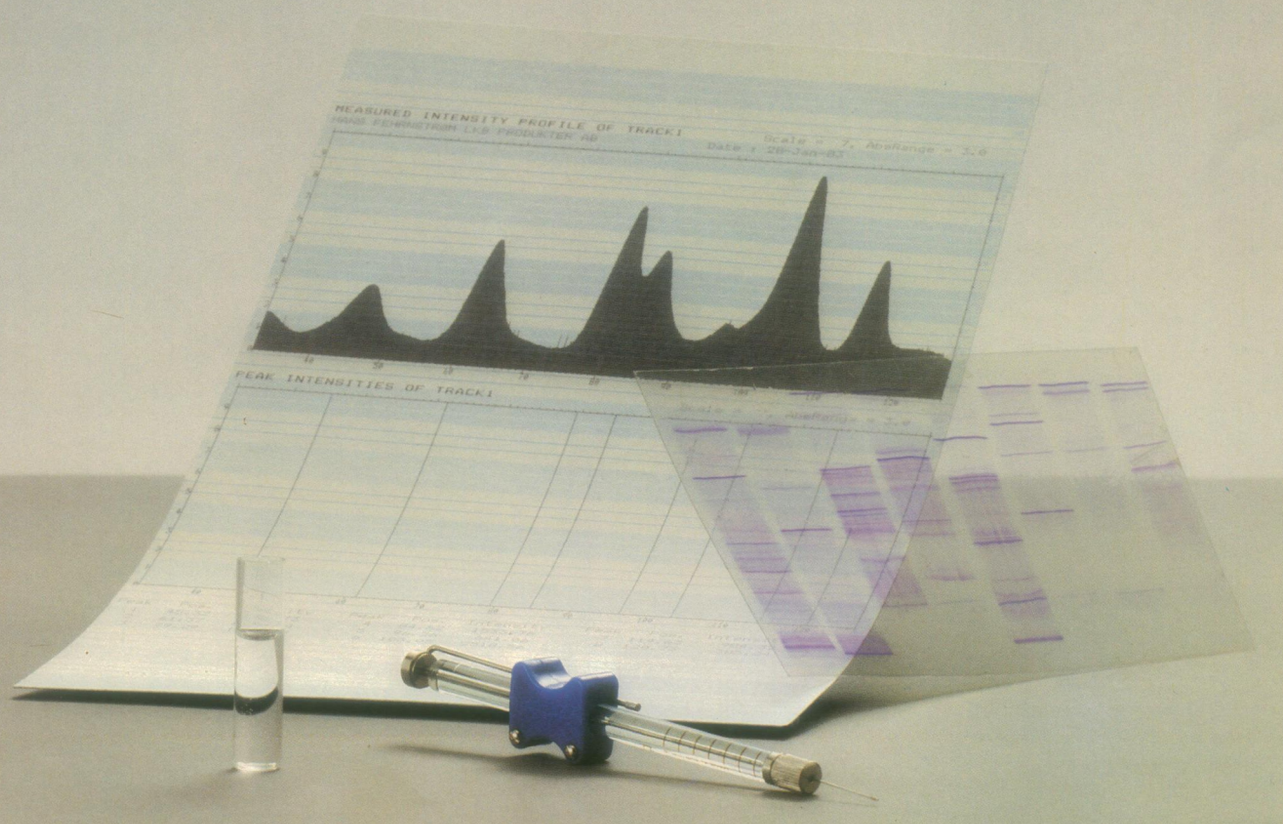


EF-DBE

asons why more than 2 out of 3 resear

gradients having a slope as low as 0.01 pH units/cm are possible, allowing you to separate proteins whose pI values differ by as little as 0.001 pH units.

Immobilized pH gradients are also completely unaffected by the presence of salts, even in concentrations as high as 0.375 M. The gradient remains linear and perfectly straight bands are obtained every time. Another striking characteristic of Immobiline gels is their combination of increased resolution and enhanced loading capacity. This makes them ideal for detecting and identifying trace components in sample loads up to 5 times those possible with ordinary gels. And since there are no soluble ampholytes to remove, high resolution electrofocusing of peptides, hormones and other low molecular weight substances is now possible.

3

HIGH CAPACITY STRAIGHT BAND ELECTROFOCUSING

Having determined the type of gel to use, the next stage in the electrofocusing system is the LKB Ultrophor. This is the first instrument designed for the professional electrofocuser, and the only such unit rated to run at 5000 volts. The compact Ultrophor performs all types of analytical and preparative electrofocusing easily, using polyacrylamide, agarose or granulated gels, thick or ultrathin, ready-to-use PAGplates or, of course, the new Immobiline gels.

Ultrophor's unique design, with interchangeable and moveable electrodes, accepts gels of any length from 1.5 to 24.5 cm. Using three electrodes you can analyze up to 96 samples in 30 minutes or less. Or you can run only one sample, and separate up to 1 gram of material. The weight of the glass lid ensures firm contact between the platinum electrodes and gels of any thickness.

The sturdy glass base of the Ultrophor is so tough you can cut gels directly on it, yet it safely supports even ultrathin gels in the presence of 5000 volts. An aluminium block ensures fast, efficient cooling, while the unique gas inlet simplifies the establishment of a controlled environment, enabling you to achieve stable gradients up to pH 10.75, uncontaminated by atmospheric CO_2.

4

CONSTANT POWER AT UP TO 5000 VOLTS

Ultrathin and Immobiline gels allow electrofocusing to be carried out at higher voltages, giving better resolution and shorter run times. LKB Ultrophor is the only unit rated for 5 kV, and to take full advantage of this we have developed Macrodrive 5: a safe, easy-to-use power supply. This adaptable unit provides constant voltage from 10 to 5000 V, constant power from 0.1 to 200 W or constant current from 0.1 to 150 mA. You select the parameter and the upper limit by simply pushing the appropriate button and dialing in the desired value.

Macrodrive 5 has been designed to meet or exceed international safety standards. It is fitted with a fast-acting ground leakage detector, deeply recessed contacts set in special one-piece plugs, and optical sensors which immediately cut off the output if the plug is pulled. The power supply is connected to the MultiTemp II Thermostatic Circulator, which automatically shuts down both units should the circulator fail.

Seven good re

1

BUBBLE-FREE ULTRATHIN GELS

Ampholine carrier ampholytes were pioneered by LKB in the mid 1960's and remain the basis of most electrofocusing applications even today. Ideal for both analytical and preparative electrofocusing, the LKB Ampholine series can be used with polyacrylamide, agarose and dextran gels, or with density gradient stabilizing media. The 14 versions produce linear gradients over the entire pH range from 2.5 to 11, ensuring reproducible separations and accurate pI determinations.

Each batch of Ampholine is carefully checked for low UV absorbance and for the absence of impurities which give rise to the staining artifacts found with other makes of ampholytes. Purified by electrofocusing, each batch is analyzed to ensure a linear and continuous pH gradient. Quality control standards are so rigorous that 99% of all users cannot detect any batch-to-batch variation. Finally Ampholine is sterilized by microfiltration in order to preserve the high quality and reproducibility.

For many applications, the convenient LKB Ampholine PAGplate and UltroPAG series allow the researcher to avoid the time and trouble involved in casting electrofocusing gels in the laboratory, while guaranteeing high resolution and good reproducibility. Up to 96 protein samples can be separated simultaneously on these ready-to-use gels, enabling users with high workloads to spend their time screening samples instead of casting gels. PAGplates are 1 mm thick, while the newer UltroPAG plates have a thickness of only 0.5 mm. These ultrathin gels permit faster separation with higher resolution, yet simplify destaining and preservation. Both types of plates are available in both narrow and broad pH ranges to suit each particular application.

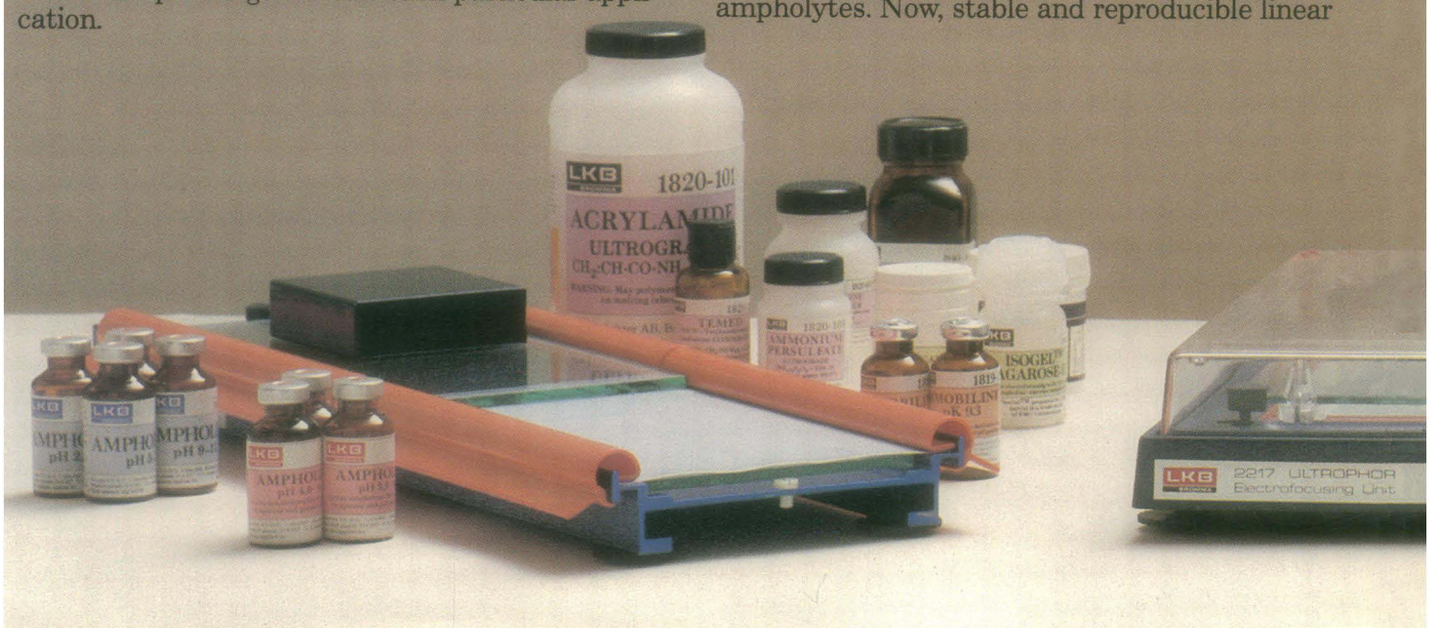
LKB also provides a full assortment of fine chemicals for electrofocusing, including the various components used in our own pre-prepared gels. Stringent quality standards are applied during the manufacture of these reagents in order to meet the rigorous demands of high resolution electrofocusing. LKB UltroGrade Acrylamide reagents are analyzed by isotachophoresis to measure charged contaminants accurately and packed in small quantities to ensure freshness. LKB also supplies two high quality grades of agarose for electrofocusing, as well as detergents, gel additives and stains, plus accessories such as glass plates, syringes, sample applicators and preserving films. And, of course, the LKB Ultromould makes it far simpler to prepare bubble-free ultrathin gels in your own laboratory, tailored to your special pH ranges.

2

IMMOBILIZED pH GRADIENTS FOR HIGHEST RESOLUTION

Another unique LKB contribution to electrofocusing, our new Immobiline system provides a genuine alternative to traditional gels. The significant difference is that the Immobiline pH gradient is an integral part of the gel, since the buffering groups which make up the gradient are covalently bound to the polyacrylamide base. The system is designed to allow you to select a pH gradient as wide as 3.0 pH units, or as narrow as 0.1 pH units, anywhere within the range 3.8 to 9.5. This tailoring of the gradient to suit specific applications permits extremely high resolution to be achieved.

The Immobiline system wholly eliminates conductivity gaps and gradient drift, thus overcoming one of the major limitations of soluble carrier ampholytes. Now, stable and reproducible linear



LKB: enhancing tradition...

Ever since LKB introduced electrofocusing in 1966, we have maintained a high level of research and development activity. In the early years much of this activity was educational, directed towards raising the awareness and increasing the general knowledge of this totally new technique. More recently, LKB's development team has co-operated with leading researchers around the world in order to increase the resolution and expand the versatility of this powerful technique.

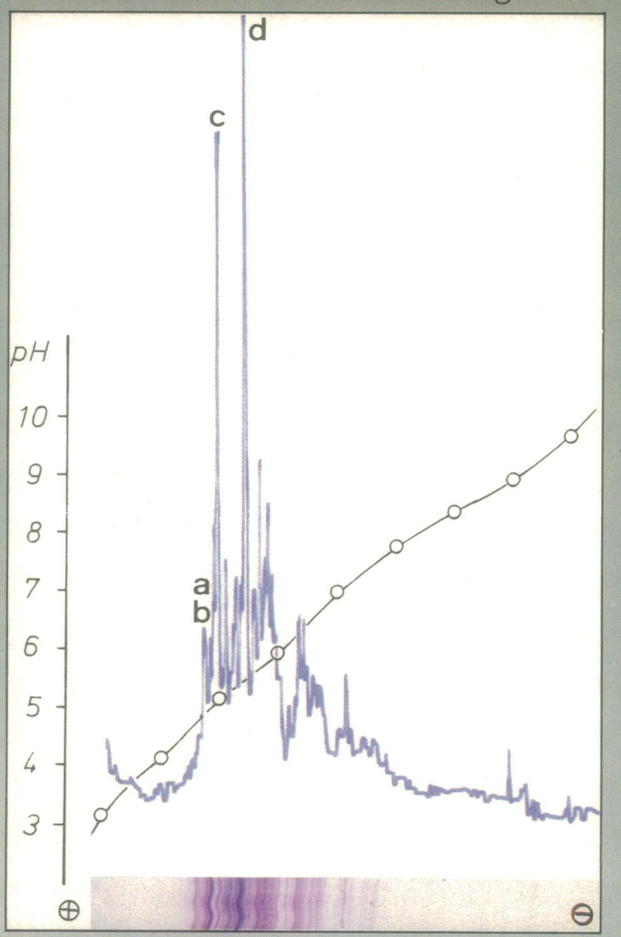
High quality gels are essential to successful electrofocusing and, while LKB supplies a broad range of ready-to-use gels, we recognize the need at times to cast gels with more specialized pH gradients. Anticipating the trend towards thin and ultrathin gels, LKB now introduces the Ultromould: a simple device designed to cast bubble-free gels as thin as 0.1 mm in less than 30 seconds. Together with our Ampholine® carrier ampholytes, the Ultromould makes gel casting quicker, easier and more certain.

LKB also provides all the other components required to make up a complete electrofocusing system. The same care and attention to quality go into the design and manufacture of our electrofocusing unit, power supply, cooling unit, laser densitometer and data analysis software. The result is a fully integrated system which gives significant advantages over and above the sum of the benefits provided by each unit alone. This is LKB's synergistic approach to electrofocusing.

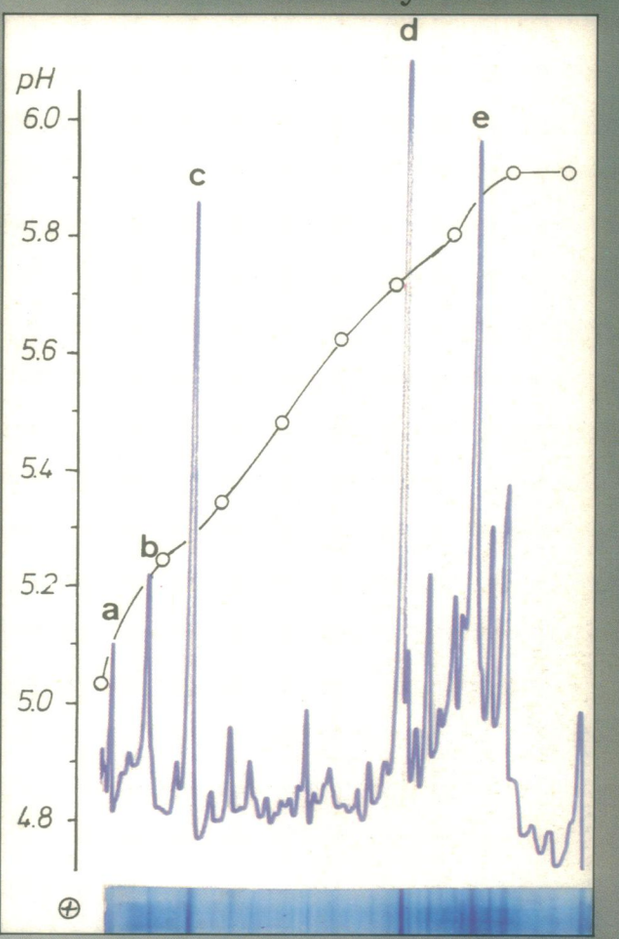
LKB'S HISTORY OF ELECTROFOCUSING
1966 electrofocusing and Ampholine introduced preparative electrofocusing in density gradients
1972 Multiphor introduced analytical electrofocusing in polyacrylamide gels
1975 ready-made electrofocusing gels, PAGplates preparative electrofocusing in granulated gel rapid, constant power electrofocusing
1977 routine clinical electrofocusing
1978 agarose electrofocusing introduced
1980 capillary-cast ultrathin gels introduced
1981 quantitation by laser densitometry
1982 immobilized pH gradients introduced

...and pioneering innovation

Traditional electrofocusing



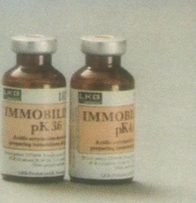
LKB Immobiline System



Courtesy of Dr. A. Görg et al., Technische Universität, München.

Even the best traditional gels have some inherent disadvantages, and it was to overcome them that LKB developed Immobiline®. We replaced conventional carrier ampholytes with immobilized pH gradients, thereby eliminating both gradient drift and conductivity gaps. This means that you can now run full length gels with pH gradients as narrow as 0.1 pH units, tailor the gradient to your particular application, and achieve resolution an order of magnitude better than was ever possible before. Immobiline gels also deliver perfectly straight bands and permit substantially higher sample loadings than conventional gels.

Not all applications require Immobiline. However, this new complement to LKB's traditional PAGplates and Ampholine carrier ampholytes represents yet another exciting innovation in electrofocusing technique.



using systems

polyacrylamide, agarose and cellulose acetate gels, micro TLC plates, autoradiography films, and even tube gels.

UltroScan is easy to use, following the simple step-by-step directions. Parameters are entered using a simple keyboard, guided by flashing lights and an LED display. The location of any number of samples from 1 to 99 can be programmed into the instrument, which can then be left to scan the entire gel on its own. These locations are identified by moving the laser scanner over the gel by means of two bars on the keyboard: the gel never moves. The output from UltroScan can be fed to a potentiometric recorder or a recording integrator, but to get the most from your results we strongly recommend the use of the LKB GelScan software package.

7

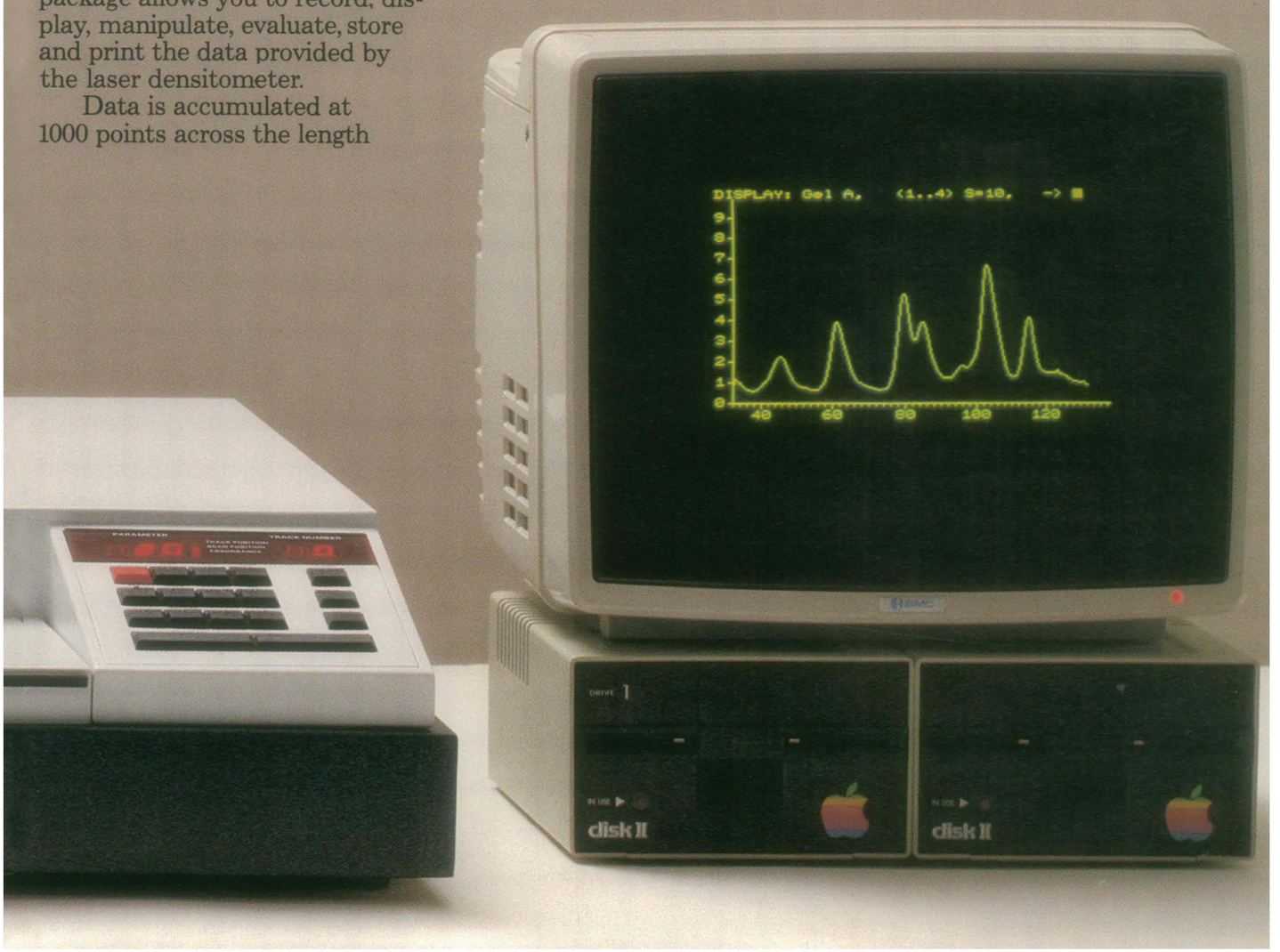
INTERACTIVE EVALUATION OF RESULTS

LKB GelScan is the natural final stage in your electrofocusing system. Written in Pascal and run on an Apple II microcomputer, our powerful new software package allows you to record, display, manipulate, evaluate, store and print the data provided by the laser densitometer.

Data is accumulated at 1000 points across the length of the scan, converted into digital form, and stored in one of the two memory areas: this use of twin memories allows you to compare two different gels. Data is displayed as a plot of intensity against position, and the software helps you to change the scale, shift the position or magnify sections of the plot.

All the peaks are accurately quantitated, even when they overlap. Peak identification is automatic, and you can add or delete unsatisfactory peaks. The position, width and height of each peak is then determined and the peak area is calculated. All measured data and calculated results are stored on disk for further evaluation or later comparison, while the printout can take the form of graphs and/or tables.

GelScan has been written so that even the researcher with little previous computing experience can easily evaluate his own data interactively, using the computer's keyboard and display. You can adapt methods to meet your own requirements, something you can never do with a fixed-program device. And GelScan ensures that you really benefit from the full potential of the LKB Integrated Electrofocusing System.



chers go on choosing LKB electrofoc

5

PRECISE TEMPERATURE CONTROL

Another important component of the LKB Electrofocusing System is the MultiTemp II combined thermostatic bath and circulator, which effectively removes the heat generated during electrofocusing. This unit provides temperature control over the range −10 to +90°C, the set temperature being accurate to ±0.5°C and precise to ±0.1°C, and is therefore suitable for many uses besides electrofocusing.

The design of MultiTemp II incorporates both pressure and suction pumps, allowing flow rates as high as 10 l/min to be maintained without the need for high pressures. The stainless steel construction tolerates coolants other than water, and safety cutouts operate in the event of low liquid level or circulator failure. Its small volume – only 2.8 liters plus the external circuit – minimizes the use of coolant, an important factor in many countries.

6

QUANTITATION BY LASER SCANNING

The use of ultrathin and Immobiline gels at high voltages has resulted in dramatic improvements in the resolution obtained with modern electrofocusing systems. Often, however, the methods used to visualize, record and evaluate these results have not kept pace, wasting many of the potential benefits. While the human eye is adequate for making qualitative determinations by inspecting stained gels, quantitative information is best obtained by the use of a densitometer.

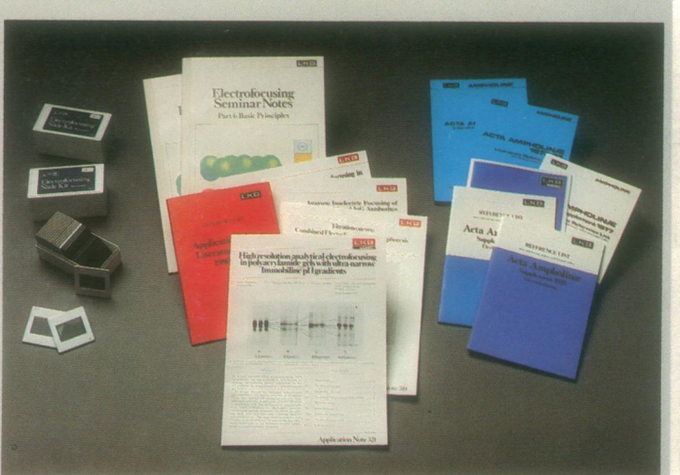
The LKB UltroScan is no ordinary densitometer; it uses a laser light source to provide the very high resolution required to extract the maximum amount of information from the latest electrofocusing gels. UltroScan has a resolution better than 50 micrometers, with excellent linearity over the range 0 to 4.0 OD. The use of a reference detector ensures very stable baselines.

Although the instrument is built around the international standard gel – the LKB Ampholine PAGplate – it can accept gels up to 105 mm long and 240 mm wide. It works equally well with

Over 5000 references speak for themselves

Now you have heard what we have to say about our electrofocusing system. But we don't expect you to just take our word for it: You can study the literature and read what others say on the subject. We have now collected published references from all over the world in the electrofocusing literature reference list, Acta Ampholinae. It's no wonder that 2 out of every 3 scientists choose LKB as their source of electrofocusing chemicals and equipment. And our continuing commitment to the development, refinement and expansion of electrofocusing is the best possible assurance of the quality and reliability of our products.

Like all LKB products, our electrofocusing system is well supported by extensive documentation of a very high standard. Application Notes and Laboratory Manuals help you get the best from your system. Twice a year, LKB News with Science Tools brings you research reports and abstracts of the latest theories and methodologies plus news of LKB product development. Our Seminar Notes and Slide Kits are invaluable instructional material, while LKB Seminars and Workshops give you the opportunity to gain additional practical experience, to exchange ideas, and to discuss your particular problems with other researchers and LKB specialists.



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