A New High-Performance Capillary Electrophoresis Instrument

This instrument automates the CE separation process with high reproducibility of analytical results such as peak areas and migration times. A diode array detector with an optimized optical path including a new extended lightpath capillary provides spectral information with high detection sensitivity. The liquid handling and sample injection systems are designed for flexibility and usability.

by Fred Strohmeier

Electrophoresis on planar gels (gel electrophoresis) has been well-known for decades as a scheme for separating sample constituents. Capillary electrophoresis (CE), on the other hand, is an entirely new type of separation methodology. The challenges for instrument design stem from the fact that the separation takes place in a capillary with an inner diameter of approximately 25 to 100 micrometers. Samples analyzed in such instruments have a volume of a few nanoliters, while the total volume of the capillary is a few microliters. Miniature dimensions like this require totally different ways of thinking in terms of technical implementation.

Project and Product Goals

When HP made the strategic decision to invest in system development for the electrophoresis market (instrument, workstation, and capillaries, including the related chemistry), it was evident that CE as a separation methodology was still in its infantile stage. It was either just being investigated or, in advanced instances, being used for new application development, for example in the search for new pharmaceutical substances. Most instruments were homemade systems composed of barely modified HPLC (high-performance liquid chromatography) equipment with an additional high-voltage power supply. Analyses were performed in an almost manual manner. As applications were developed it became obvious that instrumental imperfections were beginning to limit further acceptance of CE. Many complaints and shortcomings were stated by potential and real CE customers, who most often worked in an environment where HPLC was the method of choice for most analytical tasks. The most important limitations were missing functionality, lack of automation, not enough sensitivity, and low performance.

There were a few commercial instruments at the time, each type designed to solve a specific CE problem, but no attempt had yet been made to address all of the perceived apparatus limitations in one instrument. Before the HP instrument development was started the user needs were confirmed through numerous customer visits in different market segments. For the project team it became apparent that we had to make significant improvements in the state of the art in the following areas:

- Automation of the overall analysis process
- Detection sensitivity (ultraviolet/visible light absorption)
- Compound identification through spectral information
- Reproducibility of the analytical results (migration time, peak area)
- Usability (mainly capillary handling).

All development activities were driven by these goals. For instrumental functions that were not directly related to this priority list we tried to find an off-the-shelf solution within or outside HP.

Instrument Architecture

To provide total control over all parameters relevant to the quality of a separation, an integrated architecture was chosen. All of the functional modules such as the detector, autosampler, injection module, and capillary are within one mainframe (see Fig. l) where all of the interfaces are well-defined. This architectural approach makes it much easier to implement a single point of control concept. However, the internal structure of the instrument is modular as shown in Fig. 2.

The instrument is basically divided into two major modules: the detector module and the separation unit. They are kept strictly separate not only from a hardware point of view but also with respect to control (each has its own HP-IB interface). This structure provides the flexibility for future upgrades such as adding other detectors to the system. The coordination of the analysis, in which both modules have to be synchronized, is handled by the PC-based HP ChemStation. From there the method set up by the user is downloaded to the detector and the separation unit, and when the analysis is started the method is executed simultaneously by both modules. There is no communication between these two modules except for external start/stop, not ready, and error signals, which conforms to an HP standard for intermodule communication.

A physical connection between the modules is provided by the capillary. The inlet end of the capillary is adjacent to the separation unit, allowing the autosampler to immerse the capillary tip into the sample or a buffer. The major part of the capillary is within the cassette for thermal control purposes. Before it leaves the cassette again the capillary is guided through the optical path of the detector, where the

Fig. 1. The HP G1600A CE instrument is contained within a single mainframe and uses a PC-based HP ChemStation for control.

sample undergoes detection. The outlet end, like the inlet end, is adjacent to the separation module where the autosampler has access to the capillary tips.

Separation Environment

From a usability perspective the most critical design aspect is the way the capillary is interfaced to the infrastructure required to perform an electrophoretic separation (see Fig. 3).

Besides filling the autosampler with sample and buffer vials, the most frequent user interaction with the instrument is the changing of the capillary, either because the application has changed or because the lifetime of the capillary has expired. Before insertion into the instrument, the capillary is positioned in a forced-air-cooled cassette. This design approach has many benefits for the user. Using air as a cooling medium makes the system totally uncritical compared to a liquid cooling system whose connectors are prone to leaks. Even though liquid cooling in principle has a higher cooling efficiency, this benefit is outweighed by the fact that only highly electrically resistant cooling liquids (e.g., perfluorcarbon) can be used and these have a lower thermal conductivity than water and are very expensive. With air cooling the cassette design can be kept very simple because there are no special connectors to interface to the cooling fluid other than conduits to allow the airstream to flow through. Thus, cassettes can be exchanged without any precautions. All critical interface requirements, such as sealing the capillary against the injection vial and aligning the capillary with respect to the optical path, are shifted to the instrument where they are easier to solve. For all of these reasons the price of a cassette is very reasonable. The cassette is designed so that the detector interface is self-aligning with respect to the optical axis. The capillary ends are caught and guided into final position when the user slides the cassette into the instrument. Sealing against the fluid system is automatic.

For high-efficiency cooling, the airstream temperature is controlled using Peltier elements. The forced air allows fast equilibration of the system in case the temperature setpoint changes. The operating range is from 10°C below ambient temperature to 60°C. The temperature is sensed within the airstream. The heat exchanger temperature is sensed to measure cooling efficiency, which is optimized by adaptive control algorithms. The overall precision of the temperature control system is ±0.1°C. Because of this precision, the repeatability of migration time and peak area measurements is very good.

Detection

The detector built into the HP CE instrument is based on a UV/Vis (ultraviolet and visible light) absorption detection scheme. A diode array spectrograph provides parallel readout of all wavelengths shining through the capillary, thus

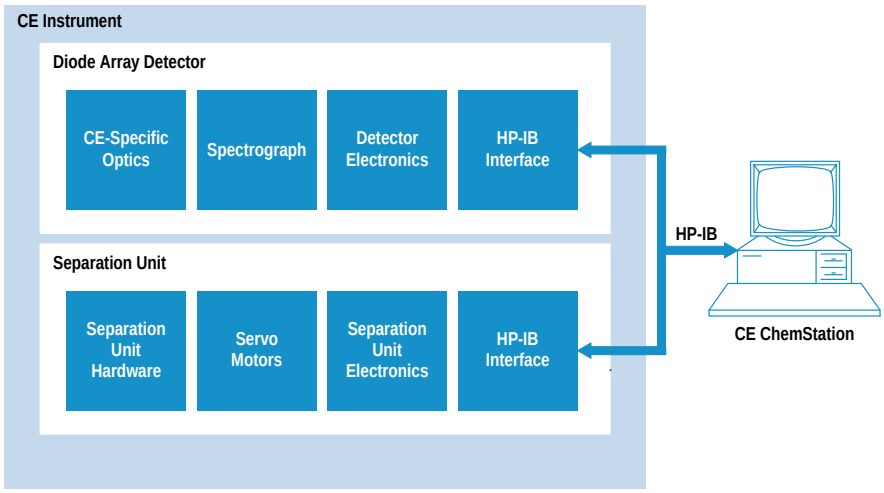


Fig. 2. HP CE instrument architecture.

Capillary Electrophoresis Applications

Capillary electrophoresis was initially regarded as an analytical separation tool for proteins and peptides. Its characteristics imply that biomacromolecules theoretically should take the biggest advantage of the technique. However, it has turned out that more then a decade after the birth of the technique the applications have spread into many more areas than just the bioscience area. In fact, for many proteins it has proven to be a bit of a problem to get a separation with the required high sensitivity using the fused silica columns. All in all this has not hindered the growth of the technique. When the first commercial instruments became available in 1990 the market was estimated to be several million dollars in size. In 1994 the expected market size might very well reach 50 million dollars. The main user groups of CE are found in the pharmaceutical market (both traditional and biopharmaceuticals), the bioscience market, and the chemical industry (see Table I).

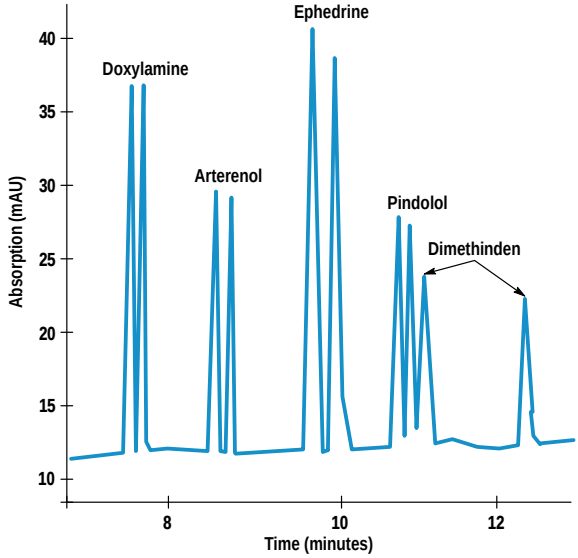
Although still mainly in use in R&D laboratories, the technique is definitely migrating towards controlled analytical laboratories such as QA/QC and product testing labs. This indicates that the technique does offer unique benefits and can expect sustained growth in the future.

Table I
CE Users

Market Segment	Estimated Share (%)
Pharmaceutical Industry	35
Bioscience	35
Chemical Industry	20
Food/Beverages	5
Others	5

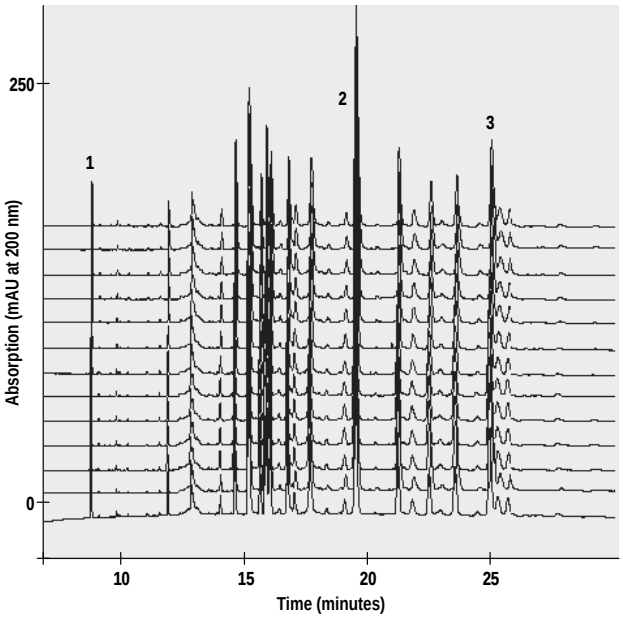
Some successful applications of CE include:

- Analysis of optical impurities (chiral analysis) (see Fig. 1)
- Tryptic digest analysis of recombinant biopharmaceutical drugs (peptide mapping) (see Fig. 2)
- DNA analysis (e.g., PCR product analysis) (see Fig. 3)
- Organic acid analysis (e.g., in beverages) (see Fig. 4).



Sample: Chiral Mixture
Buffer: 20 mM citrate, pH 2.5, 2% Carboxymethyl-β-CD
Capillary: L_{eff} = 56 cm, L = 64.5 cm, i.d. = 75 µm
Injection: 200 mbar · s
Electric Field: 300 V/cm
Detection: Signal 214.20 nm, Ref. 450.80 nm
Temperature: Capillary 20°C

Fig. 1. Capillary electrophoresis (CE) separation of a mixture of basic chiral drugs using cyclodextrin as chiral selector.



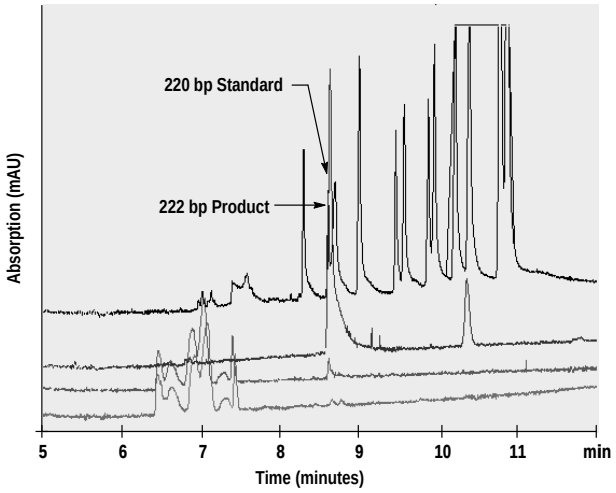
Reproducibility (%RSD)

	Peak 1	Peak 2	Peak 3
Migration Time	0.36%	0.60%	0.33%
Area	1.63%	1.89%	2.09%*

Fig. 2. Repetitive separation of a tryptic digest of recombinant human growth hormone by CE.

providing spectral information. This type of detector has several inherent features that have proved useful for many applications:

- Identification. Absorption spectra make it possible to positively identify substances by their spectral "fingerprints." The HP ChemStation controlling the instrument has a built-in spectral library. Library searches can be performed, resulting in suggestions of substances that have similar spectra. They are ranked according to a computed match factor.
- Confirmation. Spectra created by liquid chromatography separations and capillary electrophoresis separations for the same substance are, with a few exceptions, identical. Based on this, the spectra obtained with these two separation techniques are confirmatory or redundant to each other for a given sample constituent. Since the two separation techniques have different separation mechanisms it is very unlikely that a sample constituent or impurity will be missed by both LC and CE.



pBR328-Hinf 1

1.5% LPA, 6% LPA-coated
TBE pH 8.3
20 kV, 13 μA
L_{eff} = 5.6 cm, i.d. =75 μm, BF = 3
Inj: –10 kV, 3 s
260 nm (Ref 350 nm)
Capillary: 25°C
Carousel: 10°C

Fig. 3. Separation of PCR products using capillary gel electrophoresis.

Table II
CE Applications and Benefits

Application	Other Analysis Methods	CE Benefits
Chiral Analysis	HPLC, GC, TLC, SFC	Speed Easy Method Development Cost of Analysis
Peptide Mapping	HPLC	Speed Orthogonal Mechanism
DNA Analysis	Slab Gel Electrophoresis, HPLC	Superior Resolution Speed Online Quantitation

All of these applications have in common that CE offers significant benefits over previously existing techniques (see Table II).

The future outlook for CE is positive although further development of capillaries suitable for protein analysis under native conditions and the development of other detection modules such as CE-MS will be important for long-term establishment of the technique.

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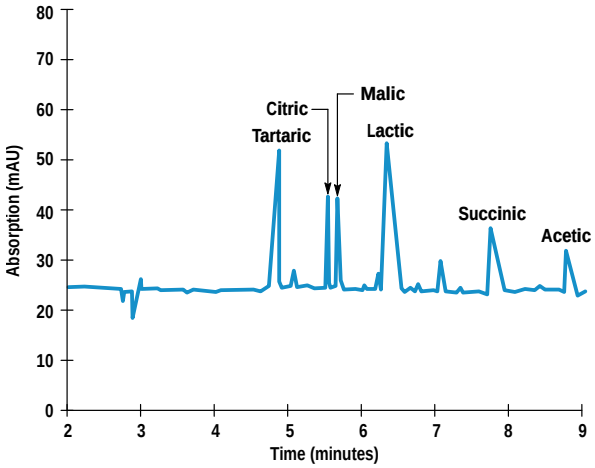

Buffer: 5 mM phthalate, 0.25 mM CTAC, 0.07% β-CD, pH 3.5
Sample: Sake (diluted 1:5 with water)
Capillary: L_{eff} = 56 cm, L = 64.5 cm, i.d. = 75 μm
Injection: 200 mbar · s
Temperature: 15°C
Field Strength: 390 V/cm, Reversed Polarity

Fig. 4. Analysis of organic acids in sake employing indirect UV detection.

- Peak Purity Measurement. The fact that a spectrum is characteristic for a certain substance can be used to measure peak purity. If the spectra sampled along the peak are identical, the peak can be assumed to be pure. If the spectra change along the peak, a second substance might have coeluted.

Even though diode array detection is a desirable feature, it would be unacceptable if the sensitivity were not competitive with conventional UV/Vis detectors such as single-wavelength detectors or variable wavelength detectors, which work with filter wheels, bandpass filters, or rotating monochromator gratings, thus providing sequential spectra. Peak widths in CE are inherently smaller than in LC. The time needed by a scanning variable wavelength detector for scanning through the full spectral range cannot be neglected. This makes these detectors less preferable for spectral identification in capillary electrophoresis. However, the sensitivity of monochromator-based detectors is viewed as the state of the art in CE.

To obtain the same level of sensitivity with the diode array based spectrometer of the HP CE system, special care was given to the optical design of the CE detector. As described in more detail in the article on page 20, the objective was to optimize the light throughput and therefore the light incident onto the photodiodes, which determines the lowest noise level achievable with an optical detector. To maximize dA/dc, where dA is the incremental absorption change and dc is the incremental concentration change of the fluid residing in the optical path, all light emitted by the lamp is focused onto the

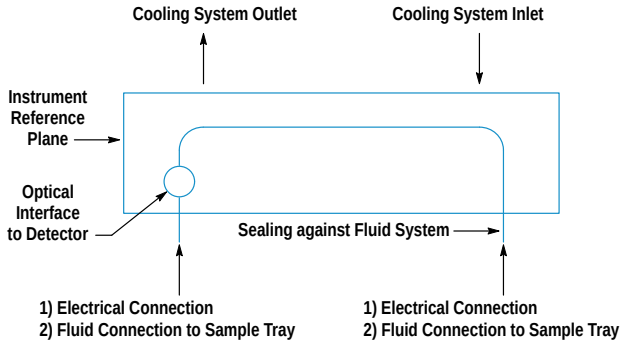

Fig. 3. Capillary interfaces to the instrument infrastructure.

capillary such that almost all rays pass through the inner diameter of the capillary and only a minimum of light (stray light) passes through the capillary wall without any interaction with the liquid inside the capillary. The benefits of this design optimization are:

- High light throughput. The result is an excellent noise level in the order of 2×10^{-5} to 5×10^{-5} AU (absorption units). This, combined with the low stray light level, provides superior sensitivity.
- Low stray light level. Besides excellent sensitivity, this results in a wide linear dynamic range, meaning that the detector responds linearly to an increasing sample concentration. The relevance of this feature can best be seen in a plot such as Fig. 4, which shows a synthetic polylysine preparation analyzed with CE.[1] The wide linear dynamic range makes it possible to quantify the smaller peaks (byproducts) relative to the main peak (active substance) very accurately.

The most remarkable feature of the detection system is the extended lightpath capillary, internally called the "bubble cell." By expanding the inner diameter of the capillary in the detection region by a "bubble factor" of BF (typically BF = 3) the sensitivity is linearly increased by a factor of BF according to the Lambert-Beer law,[2] assuming that the noise level of the detector is unchanged. This bubble cell makes the diode array detector one of the most sensitive optical absorption detectors. The larger inner diameter at the point of detection makes it possible to achieve a very low stray light level since more light rays can pass through the center of the capillary, thus increasing the linear dynamic range to 6000 (see page 23 for definition).

The HP CE diode array detector is also compatible with standard off-the-shelf capillaries. Different detector interfaces are available for the different inner diameters of capillaries with and without bubbles.

Liquid Handling

The purpose of the liquid handling functional module is to provide the necessary liquids to both ends of the capillary to facilitate a CE analysis. This includes electrolytes as well as samples, cleaning solvents, and waste vessels, as shown in Fig. 5. The module automates liquid handling so that the whole analysis can be done automatically and repetitively.

The two major design elements of the liquid handling module are the single-tray autosampler, which conveys vials to both ends of the capillary, and the replenishment system. The autosampler tray is designed so that it can position vials under both ends of the capillary independently and randomly. This enables the system to do analysis steps not possible with many other instruments.

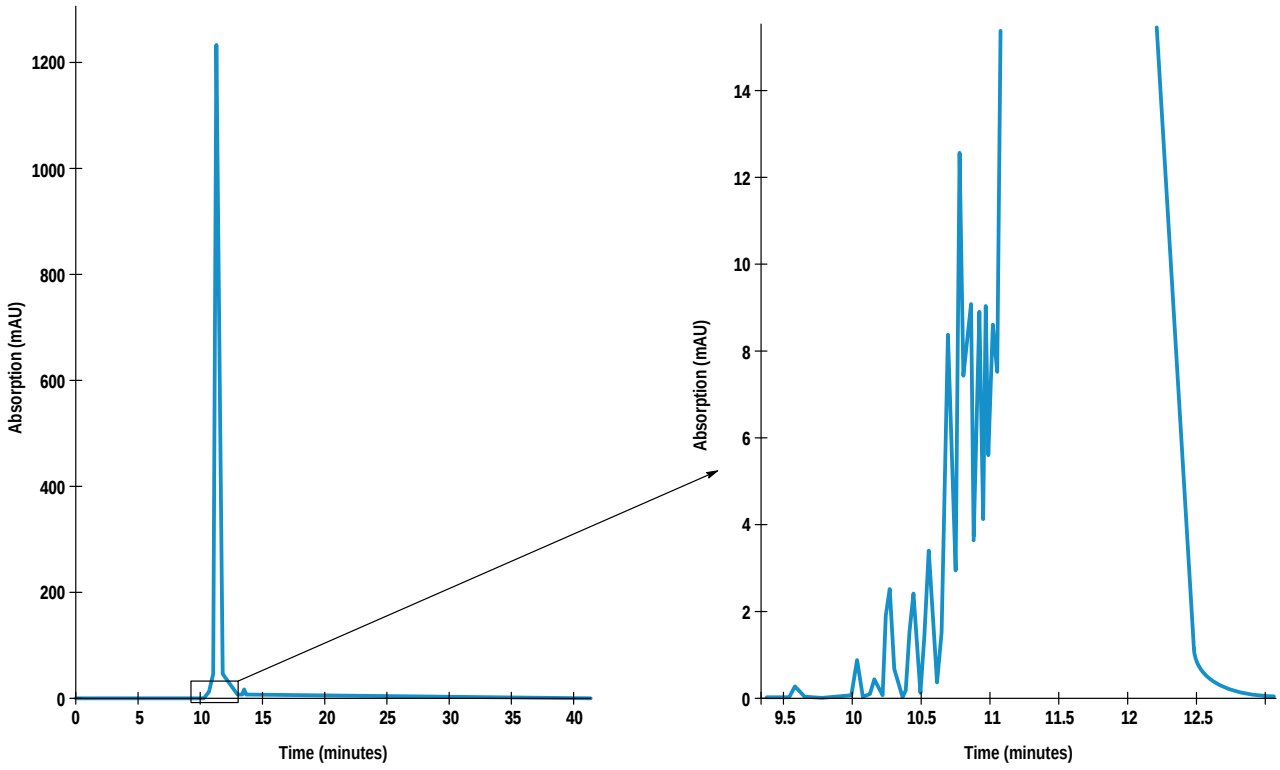

Fig. 4. Electropherogram of a synthetic polylysine preparation with 250 lysine residues.[1]

Random selection of the autosampler positions (there are 48 accessible positions) allows the user to select between sample, buffer, waste, and fraction collection vials. This gives high flexibility to the customer since the number of tray positions can be split according to the requirements of the application run on the instrument. When the same analytical method is being run in a repetitive mode, the buffer replenishment system can be employed and most positions can be filled with samples to be analyzed, thus providing maximum sample throughput.

Fractions of separated sample constituents are collected in a vial filled with a minimum volume of buffer. This is of particular importance for any further offline identification, for example with a mass spectrometer[3] or for further analysis with any other separation technique such as peptide/protein sequencing by Edman degradation.

Samples can be injected on both ends of the capillary. Usually an injection is done on the end farthest from the point of detection. However, for fast screening experiments it may be desirable to make a run on the short part of the capillary to save time. Reinjection from already collected sample fractions is also possible.

Buffer vials can be exchanged during analysis, independently on both ends of the capillary. For many applications it is mandatory to have this capability to complete a separation. For example, in isoelectric focusing mode the buffer change in pH can be used to transport the separated sample bands through the detector.

The replenishment system is primarily for the purpose of refreshing the buffers in the buffer vials by simply exchanging the contents of the vials with fresh buffer. This is required because the buffer undergoes chemical degradation by electrolysis which leads first to irreproducibility and in later stages to a shift of the pH resulting in a totally changed separation pattern. For unattended automated operation with high sample throughput, buffer replenishment is a mandatory feature, guaranteeing the highest reproducibility. Furthermore, the replenishment station adds other functions, including filling an empty vial to a selectable height or volume, emptying a vial to a selectable height, and sample or buffer dilution by adding buffer to a vial. This additional functionality also adds some basic sample preparation capabilities to the system. By ensuring the same liquid level in all vials, hydrodynamic flow effects are avoided, since no head pressure difference can occur.

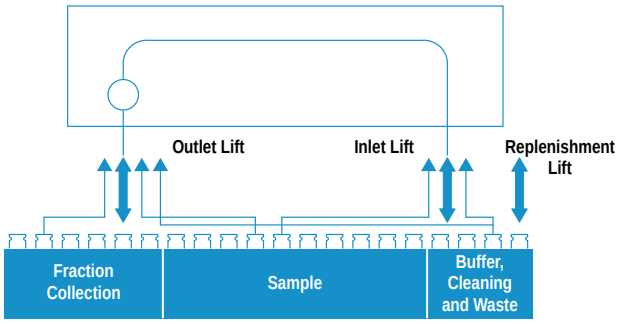

Fig. 5. The HP CE instrument liquid handling system includes an autosampler with random vial access from three lifts.

Pressure Injection

Because of the small volumes associated with CE, injection mechanisms employed in LC cannot be used in CE. For open capillaries (not filled with sieving matrices like gels) the most common injection mechanism is to apply a pressure differential across the capillaries. The volume injected follows the Hagen Poiseuille law:

$$\text{Volume} = \frac{\Delta p d^4 t}{128 \eta L}$$

where Δp is the pressure differential, d is the capillary diameter, η is the viscosity of the buffer, L is the total capillary length, and t is the time during which pressure is applied. For a given capillary the volume injected is basically the integral of the pressure-versus-time curve. The more precisely the pressure/time product is controlled, the more reproducible is the injection volume.

In the HP CE instrument the pressure/time product is controlled online and corrected immediately if any deviations are recognized from the programmed curve. Leaks in the system, which would result in a smaller injection volume, are automatically compensated by this procedure. The pressure is applied as a triangular function. On the downslope of this triangular pressure function, a vent valve is opened when the pressure is approximately equal to the ambient pressure. This has the advantage that the switching deviations of the vent valve have no significant impact on injection volume reproducibility. The pressure control algorithm significantly improves the reproducibility of the pressure injection system, as explained in detail in the article on page 50.

Pressure injection has some inherent advantages over injection by vacuum. The outlet of the capillary is not accessed during injection; this is important if other detection means like mass spectrometers are coupled to the CE instrument. Degassing and therefore air bubble formation in the capillary cannot occur, and fraction collection is much easier. Nevertheless, the design of the pressure system allows the user to apply a vacuum to facilitate injections from the detector end (shorter separation length), which may be important for fast screening experiments.

Electrokinetic Injection

Electrokinetic or electromigration injection is achieved by pulling the sample into the capillary by applying an electric field for a certain time. The quantity injected can be calculated.[4] This injection method is advantageous when viscous media or gels are employed in the capillary and when hydrodynamic injection does not work adequately. Basically, the volume injected is proportional to the charge introduced into the capillary. The HP CE instrument provides for the application of a voltage or a current for a certain time.

HP CE Technology Transfer

Looking at the new product generation process, often there is a long chain of activities involved, starting from basic research and proceeding to applied research, technology development, new product development, and finally, manufacturing. Later, while the product is being marketed, an improved and enhanced series of products will be generated in an R&D process sometimes referred to as current product engineering. Throughout this sequence of steps, knowledge, experience and competence are being built up, hopefully in a continuous, smooth, unidirectional way. However, since many people and different organizations are involved, losses, frictions, and interfacing issues associated with the transfer of know-how will occur and must be resolved or at least kept to a minimal negative impact.

Unlike the typical situation of 20 years ago, when the same group of people carried out the entire new product generation process all the way from research to manufacturing through many sequential steps, the scenarios of today's new product research and development projects have changed considerably. Given the complexity and breadth of most of HP's products, not only the analytical products, there is no way of making all of the key components entirely within HP. Instead, many things have to be acquired from external parties in various stages of development, be it fundamental research results, patented technology, methods, processes, or other know-how. In many situations even complete products or system components come from outside sources.

In our case of adding CE to the LPA (liquid phase analysis) product line, certainly we did look at the alternatives of acquisitions or external R&D collaborations, but before the final decision was made to take advantage of the accomplishments of an HP Laboratories research project and transfer technology and know-how from there to the Waldbronn Analytical Division and plunge into new product development, we had been thinking about mechanisms of technology transfer in general, and tried to reflect our conclusions in the organizational structure of our R&D function.

Generally, R&D divides its forces into activities of current product support and enhancement, development of next-generation products, and investigations, which include new products, new technology, key components, and fundamental research. The size of each of these segments depends on the business situation, which may change quickly. There is always a temptation to sacrifice the long-term investigations for short-term, market-driven problems or opportunities.

To stabilize the long-term, high-risk, but strategically important projects against the pressure of the tactical projects, we decided to divide the R&D function into two units: a smaller unit focusing on development, acquisition, and transfer of new techniques and generic components and a larger unit focusing on current and next-generation product development. The structure of the technology unit reflects the major technical and functional areas of the product line and therefore this unit has a few resident engineers and scientists who are specialists and experts in those categories. A larger number of members are set up in transient project teams and remain in the technology unit only during acquisition or investigation phases. We then transfer the project together with the transient team into the product development environment. This model should ensure minimal loss of know-how in the transfer from the investigation phase to the lab engineering phase and still keep a stable base of technical expertise and competence beyond one particular project cycle. In addition, it helps synchronize projects of different time scales and keeps the rules of the project life cycle flexible enough to adapt to new product design as well as to current product engineering.

The HP CE project was the first technology transfer project to be completed under this organizational structure and following these rules. The technology transfer from HP Laboratories to the Waldbronn Analytical Division yielded a very successful product. We have transferred technology from HP Laboratories before, but this transfer in particular went smoothly and pleasantly, I tend to believe, because of the new organizational model, but as much because of the enthusiasm, the dedication, and the support of the engineers and managers involved on both ends, including our marketing, manufacturing, and business people.

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The injection time table allows combinations of different modes of injection as well as flushing using randomly selectable vials. This makes it possible to do various sample manipulation steps that are essential for many applications. These include adding an external standard by injecting a plug of a standard compound, and adding a buffer with different conductivity to do sample stacking (enrichment) using the isotachophoresis effect.

Data Acquisition and Data Analysis

The software running on the PC next to the instrument has two major components: an instrument control module and a data collection and data analysis module.

Instrument Control. The functionality and versatility of the HP CE instrument made control by a PC the method of choice for handling the multiplicity of parameters and settings. The objective for the software design was to make the process of CE graphically visible and give the user continuous feedback on what the instrument currently is doing. As a design concept for the instrument control software an icon-based system was chosen. All instrument modules and their functions are symbolized. The user is shown a graphical representation of the instrument. Clicking on an icon displays a pop-up menu that offers the user the settings for that function. The entries are checked for plausibility and proper setting ranges. The HP ChemStation displays the status of certain events by changing colors, by showing the action taken, or by highlighting a setting the user has edited. The user can program the following parameters as functions of time:

- Replenishment
- Prerun and postrun conditioning
- Injection
- Voltage, current, and power
- Capillary temperature
- Pressure
- Inlet and outlet vial change
- Alarm limit (minimum limit for electrical current)
- Polarity of voltage or current
- Fraction collection.

For the detector, the following parameters are programmable as functions of time:

- Detector signals (defined below)
- Threshold and peak width
- Spectrum (permanent, all in peak, at up slope, peak maximum, and down slope, peak maximum, and baseline).

A feature of this software package is its simulation capabilities. It checks to see if the setup of a method to analyze a sample is in a logical sequence and if there are conflicting analysis steps such as, for example, a particular vial is needed at the inlet and outlet ends of the capillary simultaneously. When a simulation is started the graphical user interface reacts as it does during an actual run, allowing the user to follow and check online how the instrument will react in reality. Especially for complex methods, this feature helps prevent time-consuming correction steps and spillage or waste of valuable samples through wrong parameter or time table settings.

Different methods can be linked together to do a sequence of analyses. Several samples can be processed with the same method, or the same sample can be analyzed with different methods (different separation parameter settings), or a combination of both. Sequencing, together with the autosampler and the replenishment station, provides the instrument's automation capabilities.

Data Collection. The system control software collects raw data during an analysis from the following channels:

- Up to five detector signals (each signal includes wavelength, bandwidth, reference wavelength, and reference bandwidth)
- Spectrum (permanent, all in peak, at up slope, peak maximum, and down slope, peak maximum, and baseline)
- Voltage
- Current
- Power
- Capillary cassette temperature
- Pressure during run.

The first two items in this list are normally used to do the standard data analysis. For the detector signals, peak width and rise time are selectable according to the particular application. The last five data channels in the list serve the purposes of interpretation and documentation. In case of any unexpected results, this data can be used to localize and diagnose a particular problem with the instrument, the application, or the sample.

Data Analysis. When a method or sequence has been completed and the data is successfully stored on the PC, data evaluation can be performed by applying different algorithms. The information most relevant for the user consists of migration time, peak area, and peak height. When calibrated, the peak area represents a certain amount of sample. To determine the peak area, the detector signal is integrated by a built-in integration algorithm. Reproducibility evaluation of repetitive analysis with the same sample is often used to increase the reliability of the results. Besides integration, there are also built-in calibration and report generation functions. Calibration determines the unknown amount of a constituent of a known sample by calibrating with a predetermined concentration. Report generation provides different report style options including automatic spectral library searches.

One of the most powerful features of the system is its spectral capabilities. Spectra are measured using the diode array detector and stored as selected. The tools associated with spectra in the data analysis software are generally used to identify unknown compounds. The tools are:

- Spectral library. Allows a library search of selected spectra from a separation regardless of whether they are generated during an LC or a CE separation.
- Peak purity. Compares the ratio of two signals or spectra along the peak. If there is any deviation along the peak there is a probability of an overlay of two compounds.
- Isoabsorbance plot. This is for qualitative evaluation of spectral data. It can be used to generate a new electropherogram by extracting signals from spectral data, to find the optimum wavelength for detection of each component, and to average spectra to reduce noise.

Since identification by absorption spectra is a well-established tool in LC, many of the compounds analyzed with CE can be identified by available spectral libraries created with LC. The library shipped with the HP CE ChemStation software is identical to the library shipped with our LC ChemStation. This makes using the data analysis software more convenient for customers who already have experience with our LC ChemStation.

Summary

The HP CE instrument is the technical and technological implementation of the objectives stated for the project as well as for the product. Most of the requirements were implemented and can be reflected in a corresponding customer need. Significant improvements in detection sensitivity were made by the special detector design and even more by the extended lightpath capillary. The totally new liquid handling concept delivers significant automation features and versatility for future applications. The newly designed injection system provides further system reproducibility while the new forced-air-cooled cassette is a major step forward in terms of usability and flexibility. Another major advance for this type of instrumentation is the graphical user interface built into the HP ChemStation for instrument control. Finally, the electronic components and firmware developed for this product (discussed in the article on page 36) make this a functional product.

Acknowledgments

In the first place I want to thank Doug McManigill and his team from the analytical/medical laboratory of HP Laboratories for their outstanding contributions and commitment to capillary electrophoresis. To a great extent it is his achievement that HP has a product on the market. Special thanks also to Gary Gordon and his team, also from the analytical/medical laboratory, for their support and advice in the area of optical detection and for providing the crucial concept of the bubble cell. Thanks to Sid Liebes, Rich Tella, and Henrique Martins for their prompt help in the design and implementation of the bubble cell. My highest appreciation to the CE project team in Waldbronn; its commitment and dedication made it possible to finish the project on time. This includes a few individuals who were temporarily working on the project in Waldbronn, namely Henning Foukhardt, Rolf Dörrmann, Henry van Nieuwkerk, Greg Wilson, Monika Dittmann, and Sally Swedberg. Credit also to Alfred Maute

(Continued on page 19)

Industrial Design of the HP CE Instrument

It is not always recognized, and consequently not acted upon, that the contents and significance of industrial design for the success of products and the image of the company have changed in the past few years. Products have not only a technical, but also an aesthetic function. Together with some other representative features, such as advertising, company buildings, letterheads, packaging, exhibition booths, and the like, product design determines a major part of a company's image.† Today, products must not only be reliable, efficient and user-friendly, but also look like it. Visible quality today is the main attractor in many cases. In particular, the leveling out and standardization of technical achievements, even on the highest levels, lead to outward appearance being the decisive factor in the purchasing decision process more and more frequently. Last but not least, products, which also represent the company concept, have to be in line with the identity of the company. Thus, what is important is not avant-garde industrial design, but the successful combination of innovative and traditional elements.

Industrial design, therefore, is a part of product quality. Whether we thereby achieve the improvement of quality of use or acceptance among a specific target group, or capitalize on the identity of the company, proper industrial design is a sales promoting product feature. This applies not only to consumer products but also to commercial products. Very often, the first look at something determines whether we continue dealing with it or leave it alone. The quality of product design should make product quality the focus of customer interest right at first sight.

Internal Architecture

The first step towards good industrial design consists in laying out the components inside the instrument. As early as the investigation phase of the HP CE instrument project, the engineers were prompted to think about the dimensions and forms of the components they were responsible for. Rough details were then used to create all components from cardboard in duplicate. In a joint creative session, the entire project team used the models to arrange the components in multiple ways, finally deciding on one alternative. Understanding for each other's problems was gained within the team at a very early project stage: airflow and thermal problems, safety concerns, cooling, ease of use for service staff and users (which the industrial designer is also responsible for), and the like. This process not only led to the project being faster and more focused, but also had a teambuilding character.

† Image means the company as perceived by its customers. Identity means the company as it really is. Ideally, image = identity.

The immediate effects of the internal layout on the user interfaces become obvious in the vials, bottles, and cassette, which can be exchanged easily and intuitively. This ease of use is supported by the design of the instrument exterior, which visually reduces complexity.

As the project proceeded, a model of the outside cover was built (see Fig. 1). The visibility of the product in the form of the model further enhanced identification with the project, even beyond project team borders.

Appearance

Industrial design is not entirely up to the industrial designer. Carefully balancing innovative design with company-specific design within the sense of the corporate identity on the one hand, and on the other hand, emphasizing product-specific features to the best advantage, benefit both the product and the company.

The outward appearance of the HP CE instrument is designed to achieve a number of objectives:

- Emphasizing system character with a view to the HP PC, since the HP instrument is controlled by a PC. If the outward appearance of these two components is harmonized, it not only suggests that they come from the same company, but much more important, that they easily communicate with one another. In our case, this is achieved by equal use of volumes and forms as well as by HP identity elements such as coloring (bottom: dark grey, top: light), radii, HP nameplate, and power switch (see Fig. 1).
- Emphasizing system character with a view to HP analytical systems. The HP CE instrument is often to be found side by side with other HP analytical instruments in a lab or as part of an analytical system. If the outward features of our analytical instruments are in harmony with one another, this suggests to the customer that a complete solution to a problem is available from one source. In the case of the HP CE instrument, this is achieved by using, in addition to the design elements already mentioned, HP Analytical Products Group typical design or user elements such as, for example, the baseplate image, the semicircular pushbuttons set off by coloring, equal textures, equally colored windows, doors always opening in the same direction, equal status LEDs, equal fonts, and the like. The constant repetition of these visual and functional characteristics of the user interfaces makes a major contribution to ease of use by recognition. The particular challenge is always to find new solutions for new requirements that are technologically feasible but also continue the HP design tradition, so the customer finds it easy to get along and immediately accepts the solution as an evolutionary step.

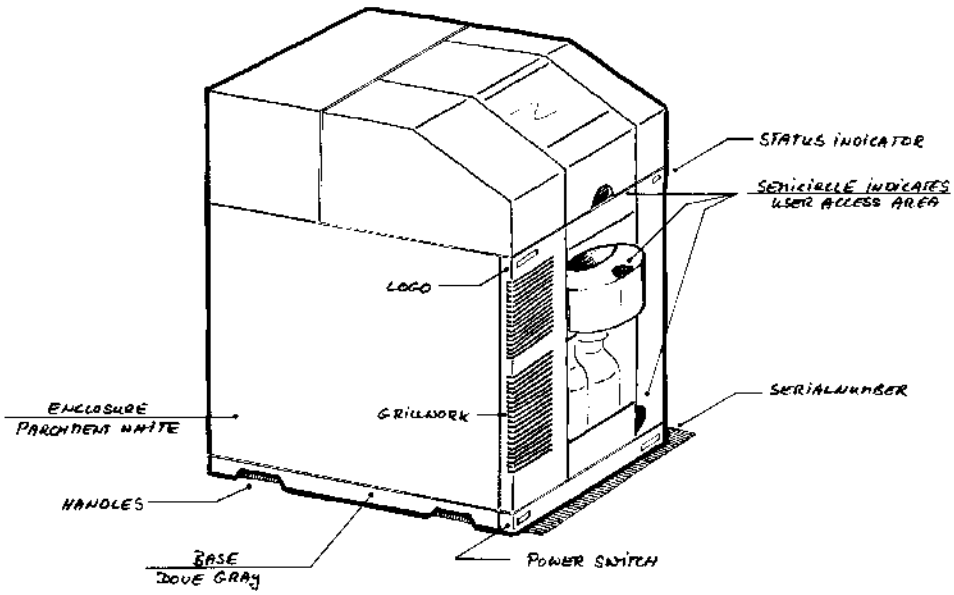

Fig. 1. Industrial design features of the HP CE instrument.

- The individual character of the HP CE instrument is emphasized by the basic instrument volume as well as by the visibility and form of some specific areas. The window parts show the areas relevant to the customer (cassette, sample tray, and replenishment bottles). Like these parts, the tray balcony, for example, is designed in such a way that it facilitates function (access to vials) on the one hand, while at the same time characterizing the look of the instrument clearly and unmistakably (and also optically reducing instrument depth). Emphasizing the vertical lines of the instrument optically supports the narrowness of the instrument.
- What is also particularly important is the visual expression of quality. Especially at a time when some instruments show only slight technological differences, customers should be convinced of the quality of our instruments at first sight. By using the right materials and manufacturing processes, we have attempted to distinguish our products qualitatively from those of our competitors, so that workmanship and finish provide our instrument with a highly professional appearance.

At the International iF Design Competition 1994, the HP CE instrument was awarded a prize for its good design and was seen by more than one million visitors in a special exhibition at the Hannover Fair and Cebit

Acknowledgments

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