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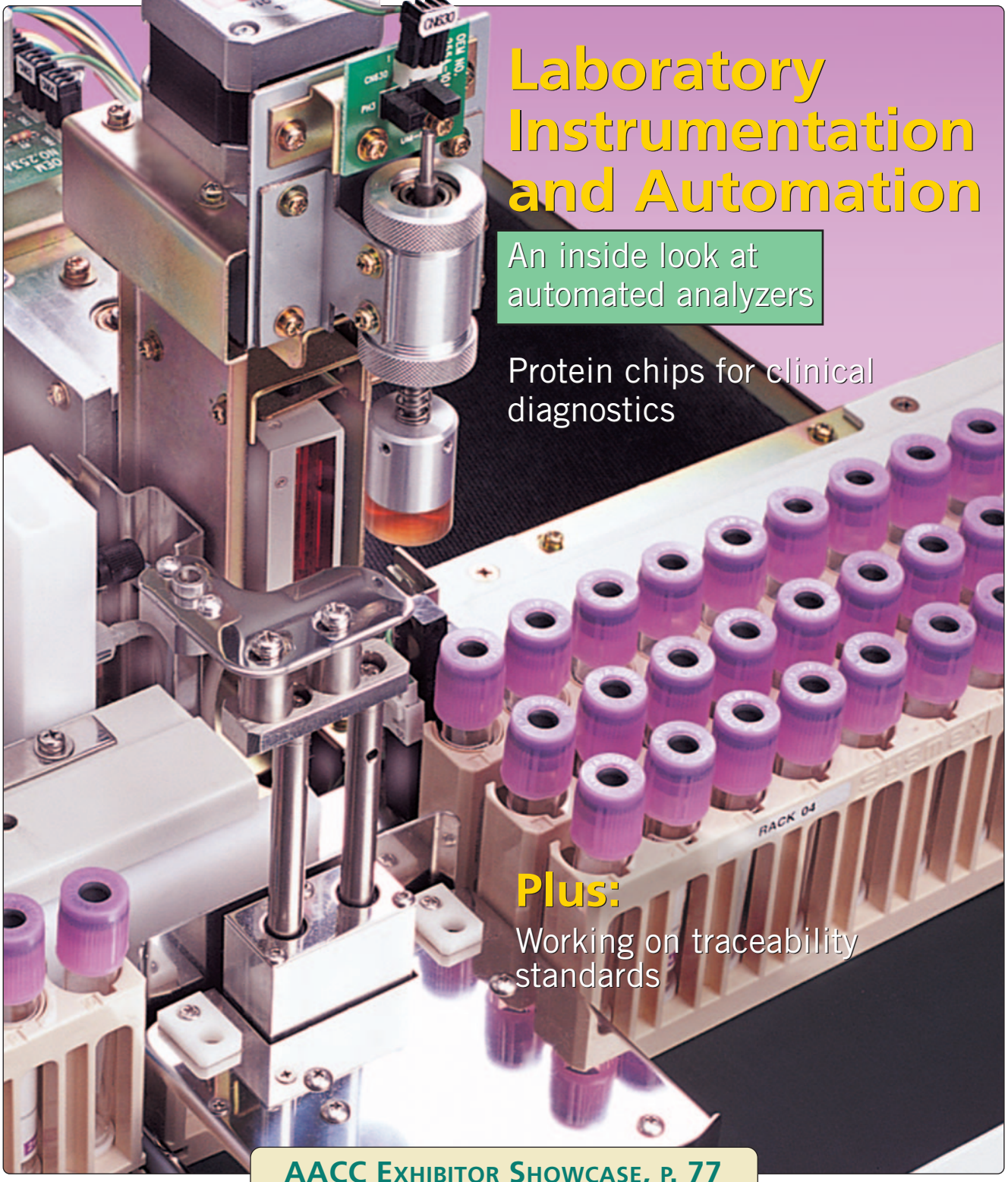

Laboratory Instrumentation and Automation

An inside look at automated analyzers

Protein chips for clinical diagnostics

Plus:

Working on traceability standards

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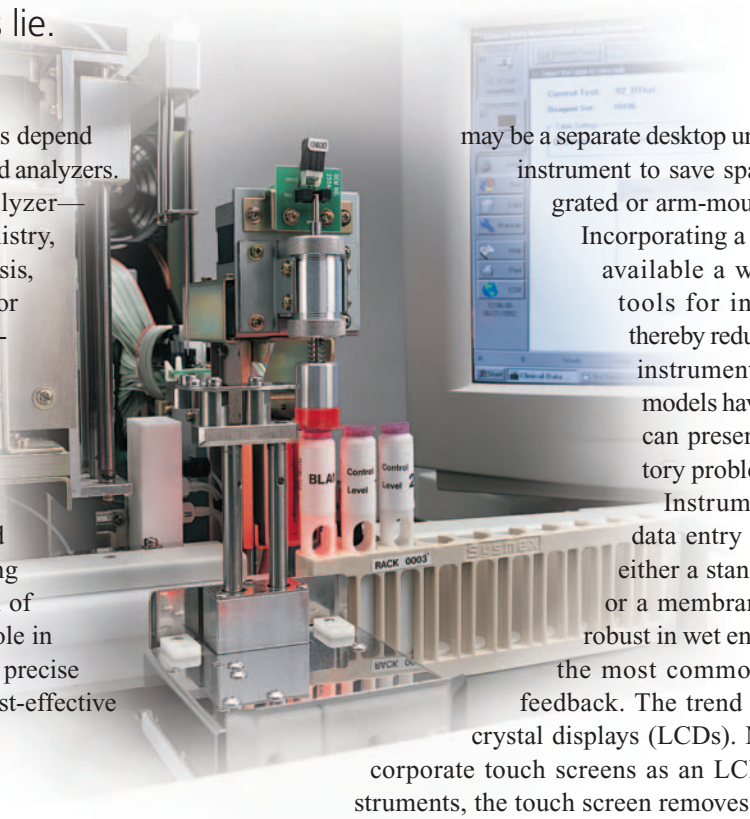
Automated laboratory analyzers analyzed

Fred Davis, Jari Palander, and John Bussell

A look under the covers of analyzer subsystems reveals where opportunities for instrument developers lie.



Clinical laboratory operations depend fundamentally on automated analyzers. The various types of analyzer—whether used for clinical chemistry, hematology, immunoassay analysis, or measurement of coagulation or blood gas—share common aspects. This article examines the five subsystems that generally make up an analytical laboratory instrument: the user interface, transport fluidics and robotics, processing elements, control and communications, and supporting electronics (see Figure 1). Each of these subsystems plays a vital role in delivering reliable, accurate, and precise results to the laboratorian in a cost-effective and timely manner.

The User Interface

Laboratorians interact with instruments for the purposes of handling data (input and output) and physically manipulating inputs and outputs. Possible elements of a data user interface are a display, a keyboard or keypad, a touch screen, a mouse or other pointing device, indicator lights, a printer, a bar code reader, a wand, and audible signals. In some instruments, interface functions are handled through a separate personal computer (PC). Others have embedded user interfaces.

Effective user-interface design is critical to instrument performance. It minimizes the risk of error and the need for dedicated operator training. Ergonomic interface layout speeds up routine activities and helps eliminate annoyances. Smooth user interactions correlate with attractive and ergonomic industrial design. Careful study of both physical and data interaction work flows by the instrument developer will result in an analyzer design that maximizes efficiency. Control interfaces can be designed for intuitive use by means of cognitive walkthroughs and usability testing.

Display and Data Entry. A PC with a Microsoft Windows operating system provides a familiar, flexible user interface. It may be a separate desktop unit or be embedded in the instrument to save space, employing an integrated or arm-mounted screen for display. Incorporating a PC in the design makes available a wide range of standard tools for instrument developers, thereby reducing development—and instrument—costs. However, PC models have limited lifetimes. This can present logistical and regulatory problems.

Instruments requiring a lot of data entry often have a keyboard, either a standard mechanical model or a membrane keypad that is more robust in wet environments. A screen is the most common means of providing feedback. The trend is toward color liquid-crystal displays (LCDs). Many products now incorporate touch screens as an LCD overlay. In some instruments, the touch screen removes the need for a separate pointing device and replaces a keyboard. Of the many touch screen technologies on the market, including capacitive, pressure, and surface acoustic wave, resistive screens dominate instrument applications.

Well-designed display and data entry subsystems expedite sample processing by providing easy access to common functions; by minimizing navigation to ancillary functions; by clearly communicating warning, status, and error messages; and by offering built-in help.

Bar Code Reading. Bar codes provide a popular tool for traceable low-error input of patient information, work lists, analysis instructions, and calibration data.[1] Bar code readers include handheld wands, handheld point-and-click scanners, and scanners embedded in the instrument. In designing instruments, developers must tackle such challenges as illegible, damaged, or missing bar codes; environmental problems, including condensation on reagent-pack bar codes; and the need for reader optics to operate reliably.

The selection of a bar code reader depends on the items to be read, the quality and type of labeling used, and the amount

of data to be transferred. Bar code readers based on light-emitting diodes are inexpensive and robust. Laser-based readers cost more but offer lower reading-error rates and better tolerance of poor label quality and label misalignment or damage.

Tubes, racks, microplates, cartridges, reagent packs, bulk fluids, and other consumables can be bar coded. Labels may be one- or two-dimensional. One-dimensional bar codes are used to encode small amounts of data—up to approximately 50 characters. Two-dimensional bar codes require higher-cost readers but enable transfer of 2000 or more characters. Common one-dimensional standards are 2 of 5 inter, Codabar, and Codes 39 and 128, while available two-dimensional standards include Codablock, Vericode, and PDF417. Prominent bar coding equipment vendors are Microscan Systems Inc. (Renton, WA), Welch Allyn Inc. (Skaneateles Falls, NY), Keyence Corp. of America (Woodcliff Lake, NJ), and Symbol Technologies (Holtsville, NY).

Loading and Unloading. Aside from data entry, most user interactions with laboratory analyzers involve loading and unloading samples, controls, calibrators, reagents, reaction vessels or cuvettes, bulk fluids, and waste containers. Making these interactions safe and efficient requires instrument design with an emphasis on human factors. Incorporating user-friendly attributes and minimizing user reliance on written instructions are key. User safety depends on smooth instrument surfaces to avoid biohazardous skin abrasion, safe operating temperatures on touchable surfaces, and ease of decontamination. Safety issues as input to hazards analysis and design review are listed in ISO standard 14971.[2]

An interesting approach to simplifying user interactions is the bold color-coding scheme used with Konelab analyzers from Thermo Clinical Labsystems (Vantaa, Finland). Subsystems for sample handling are colored red, for reagents yellow, and for consumables blue. All handles and latches are black and shaped to make their function obvious.

Sample Input and Handling. Samples of serum, plasma, whole blood, cerebrospinal fluid (CSF), urine, and other body fluids are commonly input via primary or secondary tubes, sample cups and, in some instruments, microplates. For convenient handling, tubes are grouped in racks, carousels, or carousel segments. Rack designs are generally customized to suit particular analyzers. However, the five-tube rack by Hitachi Ltd. (Tokyo) and the 10-tube rack by Sysmex Corp. (Kobe, Japan) are both used by other manufacturers' instruments.

The Hitachi five-tube rack prevents tube spillage by means of a T-slot feature that slides along rails in the input and output trays. The Synchron LX-20 clinical chemistry system by Beckman Coulter (Fullerton, CA) uses a four-tube rack that can be lifted out and hung in easy-to-clean, U-shaped input/output channels.

A critical human factors issue for instrument developers is eliminating the potential for dropped tubes and the resultant hazard of blood-contaminated broken glass. When spills do occur, it is essential that decontamination be easy and that drip flow into inaccessible areas be avoided. The BioRobot 3000 by Qiagen Inc. (Hilden, Germany) effectively addresses this concern by using a magnetic tray-movement mechanism. This noncontact approach eliminates breaks or gaps in the spill-containment area.

Instrument design also plays a pivotal role in preserving sample integrity and traceability. Maintaining chain-of-custody ensures that analytical results are correctly matched to the aspirated sample, and to batches of reagents and consumables used. Instrument developers must recognize that samples sometimes unexpectedly need to be retrieved from instruments and that users are often ingenious in their efforts to bypass interlocked covers. Simple features enforce the reading of sample and reagent bar codes at the point of aspiration and can greatly reduce the likelihood of error. A provision for controlled access—with minimal interruption of sample processing—is the ideal. One way to handle urgent interventions is to facilitate short-turnaround-time (STAT) sample addition. Rack-based instruments can allow queue jumping by STAT samples or offer a separate STAT tray.

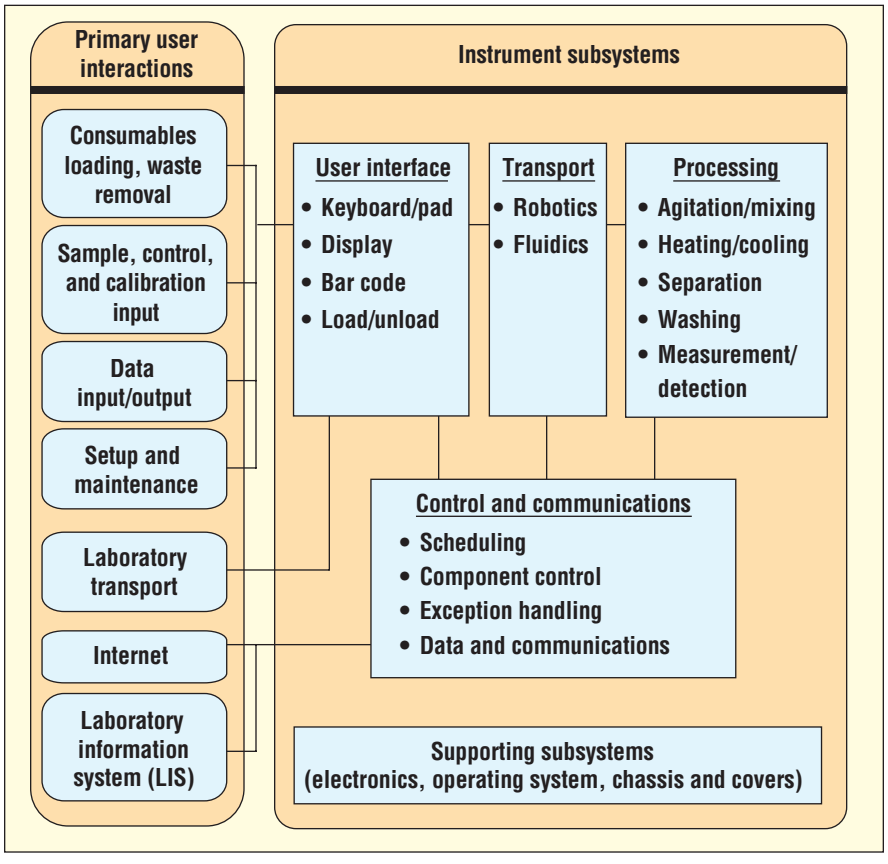


Figure 1. Interactions among the key instrument subsystems of a laboratory analyzer.

The sample-loading area should have sufficient walkaway capacity for both input and output. For random-access operation, the loading method should allow for additional samples to be placed onto the instrument at any time. These features let operators access the instrument as they need to, not as the instrument demands. A novel approach to rack loading and unloading is employed by the Variant II hemoglobin analyzer manufactured by Bio-Rad Laboratories Diagnostics Group (Hercules, CA; see Figure 2). This instrument is able to recirculate racks between input and output and hence sample or resample from any tube on board.

Transport

Fluidics. Effective fluid handling is critical to instrument performance. True quantitative results depend on highly accurate and precise aspiration and dispensing into reaction vessels, and on detection of errors due to clots and blockage. Carryover between samples should be tightly controlled, but with the smallest possible consumption of cleaning solution.

Sample and reagent aspiration and dispensing fluidics, choice of pump, design of probe tips, and control of fluid flow rates are all important considerations. Syringe pumps are the most common choice for accurate dispensing of volumes in the range of 2–500 µl. For assays requiring zero sample carryover, such as molecular technologies, disposable tips can be employed with automated tip changers.

Where carryover of 2–10 ppm or higher is acceptable, electropolished stainless-steel probes can be used in combination with air-gap separation of aspirants and priming of the pump and fluidic circuit with cleaning solution. Sometimes samples are aspirated from closed tubes such as Vacutainers, as in whole blood sampling and hematology applications; in these cases, fluidic systems and probes can be designed to pierce caps, incorporating side porting and tube-venting features.

A design consideration useful for random-access operation is to enable operators to change reagent kits, replace or top up bulk fluid containers, and empty waste containers without interrupting processing.

Figure 2. The Variant II hemoglobin analyzer from Bio-Rad Laboratories (Hercules, CA) features separate PC control and can recirculate racks between input and output.

Fluidic systems typically include liquid-level sensing to confirm that correct volumes of reagents and samples have been used for chemistry protocols. Such liquid-level sensing and blockage detection are employed to minimize carryover and dead volume for both reagents and samples. In air-primed systems, pressure feedback can be used for both level sensing and blockage detection. Fluid-primed systems normally sense liquid level by capacitive measurement, using either custom-designed circuitry or an OEM device.

Capacitive systems provide the added advantage of continuous measurement prior to entry and during aspiration and exit, thereby confirming full and correct aspiration. Electrical noise and accidental contact of the sensor with tube or cup walls can cause level-sensing errors that can be avoided by adding software that processes capacitive signals intelligently, performing real-time error checking and compensation.

Most analyzers consume bulk fluids ranging from deionized water, phosphate buffers, and carrier fluids to onboard antibacterial and cleaning agents. These fluids can be delivered through direct plumbing, operator-refilled reservoirs, or consumable boxed bladders or bottles. Inside the instrument, complex analysis protocols are supported by sophisticated fluid management systems, controlling multiple simultaneous and overlapping fluid movements. At the back end, analyzers also generate significant quantities of biohazardous fluid—as well as solid—wastes that are either stored in the instrument or directly plumbed.

Detection of the level of bulk fluids and wastes can reduce the risk of unplanned interruptions to processing, warning operators when onboard capacities are insufficient to cope with loaded sample quantities. A low-cost approach to sensing levels in bulk fluid bottles and waste containers is the use of magnetic floats with reed switches or conductive probes. Weighing fluid containers by means of strain-gauge bridges can also be effective. This process provides a continuous level signal and avoids potential failure modes associated with salt buildup, microbial growth, and even operator-induced sensor damage.

With some instruments, emptying wastes and refilling bulk containers at the beginning of each day or shift is acceptable practice. When continuous operation is required, however, a more-sophisticated fluidics design that allows bulk fluid containers to be emptied and refilled without interrupting processing is necessary. This objective can be achieved by incorporating reservoirs within the instrument. Separate internal reservoirs are used to automatically refill from bulk reagent containers and to temporarily store wastes that are later emptied into removable waste containers. Reservoirs should be sized to support processing of all onboard samples should replacement of the removable container be delayed.

Robotics. Robotic systems are used for handling samples, reagents, and wastes, for moving reaction vessels between processing stations, for manipulating consumables, and for moving instrument covers.

Sample handling includes movement into and out of the instrument and the reading of bar codes on tubes, racks, and

microplates. It also encompasses x-y-z or z-theta aspiration probe movement and the conveyance of samples to reaction vessels, analytical columns, or chambers. BioRad's Variant II has a mechanism that combines closed-tube sample aspiration with tube-cap detection, tube-height detection, tube spinning (to mix whole blood), and bar code reading.

Instrument robotics and control systems can be interfaced with a laboratory automated transport system (LATS) for sample input. A LATS may either be proprietary, connecting only selected analyzers together, or have an open architecture, providing connectivity among a wider range of analyzer brands. Linkage of robotics with such a system is an important element of instrument development. The recent introduction of a series of standards for laboratory automation potentially makes this easier, although LATS compliance with the standards is currently patchy.[3–5]

Reagent handling involves indexing carousels or rows of containers for access by reagent probes. Other functions include reading reagent-pack bar codes, agitating samples, piercing packs, and uncapping and recapping. In batch, linear, or sequential analyzers, robotic systems generally move reaction vessels or cartridges through a set of processing stations, but in random-access analyzers, they may need to be more flexible, moving reaction vessels through a variety of protocol-dependent processes.

Analyzer robotics tend to fall into two groups: adapted off-the-shelf systems such as x-y-z robot autosamplers and custom-designed robotic subsystems used in most mainstream clinical chemistry and immunoassay analyzers. Adaptation of off-the-shelf systems is more common with emerging technologies, where possibly higher instrument cost and suboptimal performance are a trade-off for an accelerated time-to-market. Custom robotics are often employed in order to minimize instrument cost, achieve high throughput, or facilitate random-access functionality.

Designing custom robotic systems presents numerous challenges. Frequently used subsystems should be placed at the front of the instrument for easy access. At the same time, the layout of related robotics must provide access for cleaning such that risk of accidental damage to delicate items like probes is minimized. Rack-handling systems need to offer easy spill cleanup and easy access for loading and unloading racks and tubes, along with the ability to carry groups of racks in trays. Reagent carousels should be small enough for convenient handling yet large enough for lengthy walkaway time and onboard storage of occasionally used reagents. Electronics should be organized in convenient modules or cards configured for simple service access and replacement. Custom-designed microprocessor motion control is necessary in configuring mainstream analyzers for economical smooth, rapid, precise motion with quiet operation.

To increase performance while reducing cost requires innovating to combine functions or carry them out in new and different ways. One example of this is the multifunction Variant II sample-aspiration robot. Another is the SL50 head from Vision BioSystems (Mount Waverley, Victoria, Australia), which detects the presence of a glass slide, manipulates it, and uses a laser to read the bar code (see Figure 3).

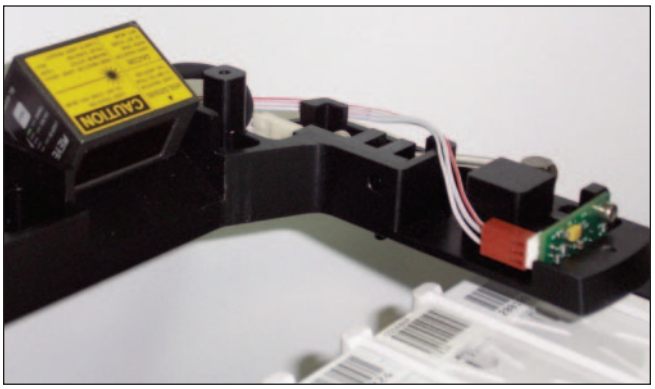


Figure 3. A system that features an innovative combination of robotic functions in glass-slide handling is the SL50 by Vision BioSystems (Mount Waverley, Victoria, Australia).

Processing

Analyzer processing steps vary with the nature of the assay or the measurements being performed, but the functions of agitation, temperature control, separation, and measurement or detection are common to many analyzers.

Agitation and Mixing. Ineffective agitation and mixing can result in low assay sensitivity and precision. Mixing sufficiently to combine reactants can often be achieved during the dispense process by means of repeated aspiration and dispensing, lateral probe movement, or ultrasonics. For applications requiring fast and extensive mixing, some systems are equipped with dedicated robotic mixers that are placed in the reaction mixture and automatically washed between uses.

Where processing utilizes particle or bead suspensions for analyte capture and separation (as in many immunoassay instruments), the suspensions may require regular agitation in reagent containers and also during assay reactions in order to maintain homogeneity. This ensures that active bead surfaces are exposed effectively to samples and conjugate reagents.

Temperature Control and Incubation. Most clinical chemistry and immunoassay analyzers need sample-incubation temperatures to be maintained accurately at around 37°C, while some of the molecular research and diagnostics instruments call for thermal cycling between 37° and as high as 95°C. Design challenges here involve keeping sample temperature within very tight tolerances during incubation and transport between processes, and minimizing sample evaporation. Incubation temperature is commonly kept stable by means of fan-forced warm air, a warmed metallic heat exchanger, or a warm-water bath. Forced-air incubators are simple but require careful design to ensure temperature uniformity. Water baths provide high rates of heat transfer but are subject to leaks and require agents to prevent bacterial growth.

Prior to processing, reagents can be cooled onboard, typically

Measurement Technology	Clinical Chemistry	Immunoassay	Hematology
Ion selective electrodes (ISE)	33	—	—
Photometry	58	22	—
Turbidimetry	11	1	3
Luminescence labeling	—	22	—
Fluorescence labeling	—	19	—
Radio labeling	—	1	—
Laser light scatter	—	1	20
Volumetric impedance	—	—	47

Table I. Measurement technologies used in a set of 171 laboratory instruments surveyed (58 clinical chemistry, 55 immunoassay, and 58 hematology analyzers). Source: ECRI.

at 4° to 12°C, to aid stability and extend their storage life in the instrument. Cooling is provided via Peltier elements or small vapor-compression-cycle refrigeration units.

Thermal sensing for temperature-control feedback is usually performed by thermistors owing to their low cost, robust characteristics, and sensing-circuitry simplicity. Biomedical chip-grade thermistors do not require individual characterization and are inexpensive and widely available. To guard against sensitivity drift or sensor failure, sensors can be installed in pairs, with software being used to compare readings and raise a warning if sensor disagreement exceeds specified limits. In damp locations or where spills may occur, it is generally best to use glass-encapsulated sensors seated in a steel tube in order to prevent moisture ingress affecting thermistor performance.

Separation. Immunoassay protocols exemplify the need for liquid- and solid-phase separation. Separation can be performed by capture on a solid phase attached to reaction-vessel walls (as in traditional enzyme-linked immunosorbent assay techniques), followed by fluid extraction and washing.

An increasingly common approach is to capture analytes with immunoreactive coated superparamagnetic beads. Magnetic-field gradients are then used to immobilize the beads during washing, leaving the analytes on them behind for subsequent processing steps. A more unusual approach is taken with the Immulite 2000 analyzer (Diagnostic Products Corp; Los Angeles), which uses a single large bead as the solid-phase substrate and spins the reaction vessel without magnetic separation in order to decant surplus liquid phase.

In some systems designed to work with very small sample volumes, capillary electrophoresis is a preferred method, combining transport and separation. Using the properties of captive ions on capillary walls plus the application of a high-voltage dc field across the direction of transport, electrophoresis produces a plug flow of reagents and buffers. Analytes of differing mobility are separated during transport, facilitating sample analysis via detection of mass and charge properties. Electrophoresis requires careful design. Buffers, reagents, and samples must be matched so that overheating, evaporation, and denaturing of reagents and samples in the electric field are avoided.

Measurement and Detection. Every analyzer is based on a measurement or detection technology closely related to assay and chemistry development. A wide variety of technologies exist. Depending on applications, instruments can incorporate more than one measurement technique (see Table I). The choice of detection technology can be a primary source of competitive advantage.

Photometry and ion-selective electrodes (ISEs) form the basis of most automated clinical chemistry analyzers. Both well-established techniques routinely deliver robust, reliable performance with a wide range of systems. They often serve together on a single platform to cover the spectrum of clinical chemistry assays of interest. ISEs use a semipermeable ion-selective membrane to generate a voltametric response to the activity of targeted ion species. Electrolytes measured are typically sodium, potassium, and chlorine. ISE systems tend to exhibit calibration drift with time; thus, provision for automatic recalibration at regular intervals must be considered when designing ISEs into automated analyzers.

Automated clinical chemistry assays involve conventional photometric absorbance measurements of the color change induced by reaction of the reagent with the target analyte. These systems employ a simple tungsten light source, with interference filters or a grating spectrometer to provide spectral resolution. In most cases, absorbance measurements are made at several wavelengths and correlated through a calibration equation to correct for interferences and background.

Certain clinical chemistry or immunoassay reactions give rise to agglutination. Precipitated particulate reaction products suspended in the specimen can be measured by turbidimetry or nephelometry. Turbidimetry determines the concentration of these suspended particles by detecting a decrease in beam transmission from an optical probe (obscuration) and nephelometry by measuring the increase in scattered-light intensity. Turbidimetric measurements can be made with a conventional photometer; consequently, most chemistry analyzers offer some turbidimetric immunoassays as an adjunct to their clinical chemistry menu.

Many modern high-sensitivity immunoassay analyzers employ luminescence or fluorescence detection techniques. Both these methods measure the intensity of optical emissions from labeled molecules that attach to the analyte species during the immunoassay reaction. Fluorescence techniques stimulate light emission from a fluorescent label by means of a powerful excitation source such as a xenon flash or laser.

Chemiluminescence-based instruments stimulate light emission through a chemical reaction between the label and a luminescence activator added to the sample at the end of the

assay process. A wide variety of luminescent molecules are used, although most are based on the oxidation of enzymes such as peroxidase, glucose oxidase, or alkaline phosphatase. Emitted light intensity is proportional to the amount of bound label and provides a measure of analyte concentration either as peak or integrated emission intensity. Because of their overall higher sensitivity, chemiluminescence-based analyzers are more widely used than fluorescence-based instruments.

Hematology analyzers count and classify cells via either laser scattering or measurement of electrical impedance change caused by single cells passing through a small orifice.

Control and Communications

The complexity of instrument control and communications depends on the number of subsystems running at once and the amount of data processed and exchanged. Complexity increases significantly when multiple protocols are operating simultaneously in random-access mode, as in large clinical analyzers, and also when the performance of particular protocol steps must be monitored and verified.

Instrument Control. Instrument electronics provide the processing power and real-time performance needed for low-level control of individual hardware devices such as robotics. Control software interfaces with this physical hardware at a lower level while communicating with the user interface and other systems, such as the LIS, at a higher level. OEM single-board computers have become a popular control platform for analyzers, providing support for a range of operating systems; development and user-interface tools; data management options; and interfaces for communications.

Another common alternative is to develop custom control platforms from economical embedded microprocessors and digital signal processors. To improve reliability and flexibility, the number of cable harnesses can be reduced by off-loading some real-time monitoring and control functions to distributed dedicated processors. For example, smart stepper motor drivers can monitor and control robot motions, undertake automatic error recovery locally when faults are detected, and then advise the central controller of the outcome.

Scheduling. When analyzers perform predefined steps in a sequential assembly-line manner, scheduling and control of instrument functions is relatively straightforward; a simple serial (clockwork) algorithm can be used. But complex real-time scheduling is necessary to coordinate instrument actions when various assay protocols are run concurrently, because work lists for samples are continually received.

Subsystem activities need to be scheduled in order to avoid conflicts that might otherwise occur when different assays and patient samples require attention from the same subsystems simultaneously. More-sophisticated scheduling algorithms employ techniques such as constraint logic programming to regulate traffic flow, achieving shorter times to first result with the same hardware.

Exception Handling. Analyzers can be temperamental. Operators may do unusual things, and complex mechanisms do not always function reliably. To handle these challenges and maintain reliability, high-quality analyzers incorporate intelligent exception-handling software. In response to abnormal situations, this software performs automatic error recovery, guides the user through intervention actions to achieve recovery, and pinpoints possible sources of error to aid in fault diagnosis and correction.

Implementing effective exception-handling software increases instrument uptime; reduces loss of samples, consumables, and results; and minimizes the need for operator interventions and service calls. Among the problems an exception-handling system can address are power failures and brownouts, LIS communication glitches, operator errors, unscheduled operator interruptions, problems with samples and consumables, missing or damaged bar codes, malfunctioning robotics, and shifts in calibration. Almost half the software written for complex analyzers may be devoted to error detection, prevention, and correction.

A critical purpose of exception handling is to protect samples and ensure the integrity of results. If a sample cannot be processed correctly, the instrument must alert the operator so that corrective action can be taken, avoiding sample losses or inaccurately reported results. Examples of appropriate exception handling in this situation would be detecting blood clots that have prevented a full sample from being aspirated and warning the operator when an incubation temperature or processing time has been exceeded.

Communications and Data Management. Clinical analyzers must interface with a variety of third-party systems, including printers, LISs, LATSs, databases, and quality-assurance systems. Most computer platforms and operating systems support a wide range of communication interfaces, including RS-232 and universal serial bus (USB), and protocol layers such as HL-7, transmission control protocol/Internet protocol, Bluetooth, and IEEE 802.11.

Analyzers typically store operational data—such as their hardware configuration—and event logs in order to facilitate service diagnosis. Outputs from the measurement and detection system can be analyzed onboard or communicated via an interface to an external PC. The primary function of an analyzer is, of course, to produce results data. These are typically matched with patient data and with related quality control information (e.g., operator identity, time and date of analysis, and reagent batches used), providing detailed output for local storage and display, and for remote data storage.

Internet Connectivity

The Internet is revolutionizing the way instruments are developed and operated. Via the Internet, developers can control prototype instruments, monitor their behavior, and download new software to enhance performance. They are able to work collaboratively around the clock, easily sharing documents and data across many time zones. Using video links, instrument developers can share expertise and review ideas with product managers, biochemists, service personnel, and ap-

plication specialists.

The same enabling technology is now an integral part of latest-generation laboratory analyzers. The Hopkins point-of-care testing software system, for example, collects data from geographically dispersed hemoglobin analyzers and monitors thousands of glucose and hemoglobin meters.[6] Beckman Coulter, Bio-Rad Laboratories, Dade Behring (Deerfield, IL), Diagnostic Products Corp., and Ortho-Clinical Diagnostics (Raritan, NJ) analyzers already offer remote service diagnostic features.[7]

And new frontiers are being explored. The latest version of Clinical Systems Network (CSN) software released by Bio-Rad Laboratories for the Variant II HbA1c testing platform enables instruments to be connected with the Internet, improving both user and service support. Up-to-date quality control information, training materials, and assay and operator manuals are available on-line. Video monitoring technologies simplify user training and provide immediate troubleshooting assistance.

Running directly on laboratory analyzers, Internet applications help build user knowledge and experience, creating worldwide virtual communities. The CSN Variant Online Library, for example, facilitates distribution of abnormal hemoglobin chromatograms throughout the hemoglobin testing community. Internet-enabled systems can provide secure sockets layers (SSL) encryption and digital certificates for user security.

Internet connectivity not only enhances the role of analyzers in healthcare delivery, but it can also increase instrument uptime and reduce service costs.

Conclusion

This article has taken a look at some of today's analyzers. What will be found inside tomorrow's analyzers is uncertain. New commercial testing technologies are making their way from research-only to regulated point-of-care and laboratory analysis applications. These emerging technologies will radically change the way testing is performed, in some cases moving analysis out of the laboratory and in others enhancing the cost-effectiveness of centralized laboratory testing. In new growth markets, such as molecular diagnostics, instrument developers will play a pivotal role in overcoming technical hurdles.

In established markets, instrument developers and manufacturers will be focusing on making analyzers better, faster, and cheaper. Critical performance parameters such as reliability, accuracy, sensitivity, and throughput will undoubtedly be increased, and automation will continue to eliminate manually intensive activities for operators, reducing errors and removing hazards. Design innovations and new technologies can be counted on to deliver improved instrument performance and lower per-test costs.

References

1. RC Palmer, *The Bar Code Book: Comprehensive Guide to Reading, Printing, Specifying, and Applying Bar Code and Other Machine-Readable Symbols* (Concord, NH: Helmers, 2001).

2. *Medical Devices—Application of Risk Management to Medical Devices*, ISO 14971:2000(E), Annex A (Geneva: International Organization for Standardization, 2000).

3. *Laboratory Automation: Communications with Automated Clinical Laboratory Systems, Instruments, Devices, and Information Systems*, NCCLS Standard AUTO3-A (Wayne, PA: National Committee for Clinical Laboratory Standards, 2001).

4. *Laboratory Automation: Systems Operational Requirements, Characteristics, and Information Elements*, NCCLS Standard AUTO4-A (Wayne, PA: National Committee for Clinical Laboratory Standards, 2001).

5. *Laboratory Automation: Electromechanical Interfaces*, NCCLS Standard AUTO5-A (Wayne, PA: National Committee for Clinical Laboratory Standards, 2001).

6. M Taylor et al., "Opening the Door to a Laboratory Without Walls," *American Clinical Laboratory* 19, no. 6 (2000): 12–13.

7. A Reder, "Remote Diagnostics for Laboratory Instruments," *IVD Technology* 7, no. 1 (2001): 32–40.

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