

LabVIEW Interface Tests Pharmaceutical Products

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The Challenge: Developing a software interface for an RS-232-based, 64-channel kinetic spectrophotometer, used for endotoxin analysis in the medical and pharmaceutical industries.

The Solution: Using LabVIEW, we simplified the sample tracking and analysis procedures necessary in this project.

When Atlas Bioscan Ltd required a software interface for its ATi-6000 Kinetic Spectrophotometer, National Instruments Alliance Program Member Process Analysis & Automation recommended LabVIEW.



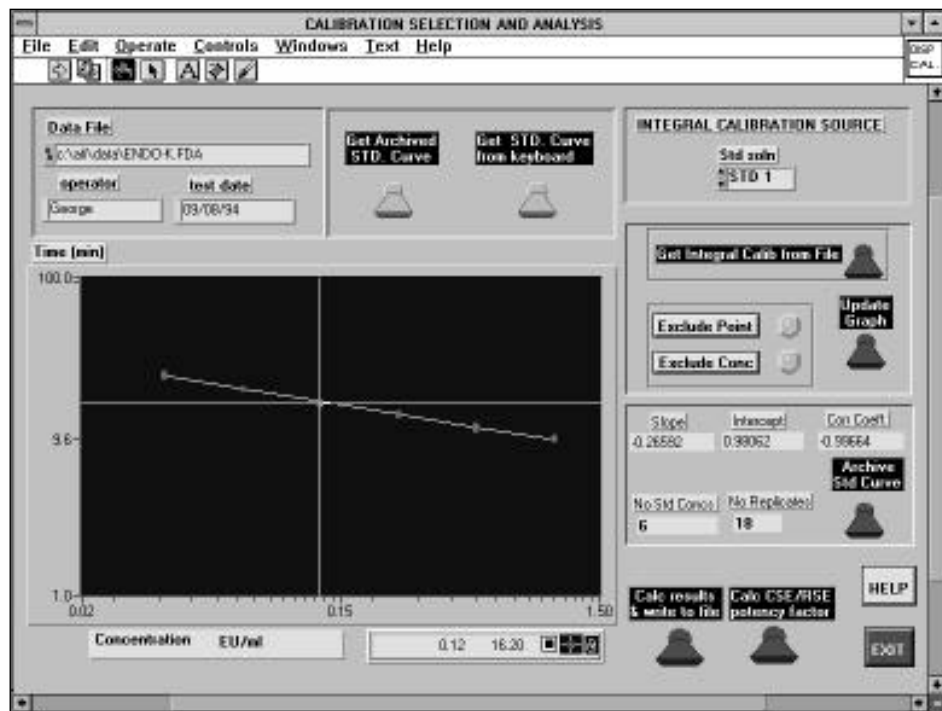
The ATi-6000 consists of 64 8 mm wells machined into an aluminum incubation block, which is homogeneously heated by an element that is equidistant from each well. Fibre optics couple light from a visible optical source to test tubes located in each well. Photo diodes measure the optical density transmitted through each tube and profile the absorption of light against time.

Development of the system was inspired by the requirements of endotoxin analysis in the medical and pharmaceutical industries. With its design, however, the system can be used in a wide range of general-purpose, analytical procedures where an analyte concentration in a solution is a function of the optical transmission of light through the solution. Application areas include end-point testing,

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immunoassay, cytotoxicity, microbiology, clotting factors, and food science.

By developing the software in LabVIEW rather than a conventional programming language, we completed the package quickly. We developed two discrete versions of the software. The first is a general-purpose package to log and



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analyse colorimetric and turbidimetric kinetic reactions by profiling optical density changes with time. The second and most recent version of the product is for the specific purpose of endotoxin analysis according to procedures laid down by the U.S. Food and Drug Administration (FDA).

Endotoxin Analysis

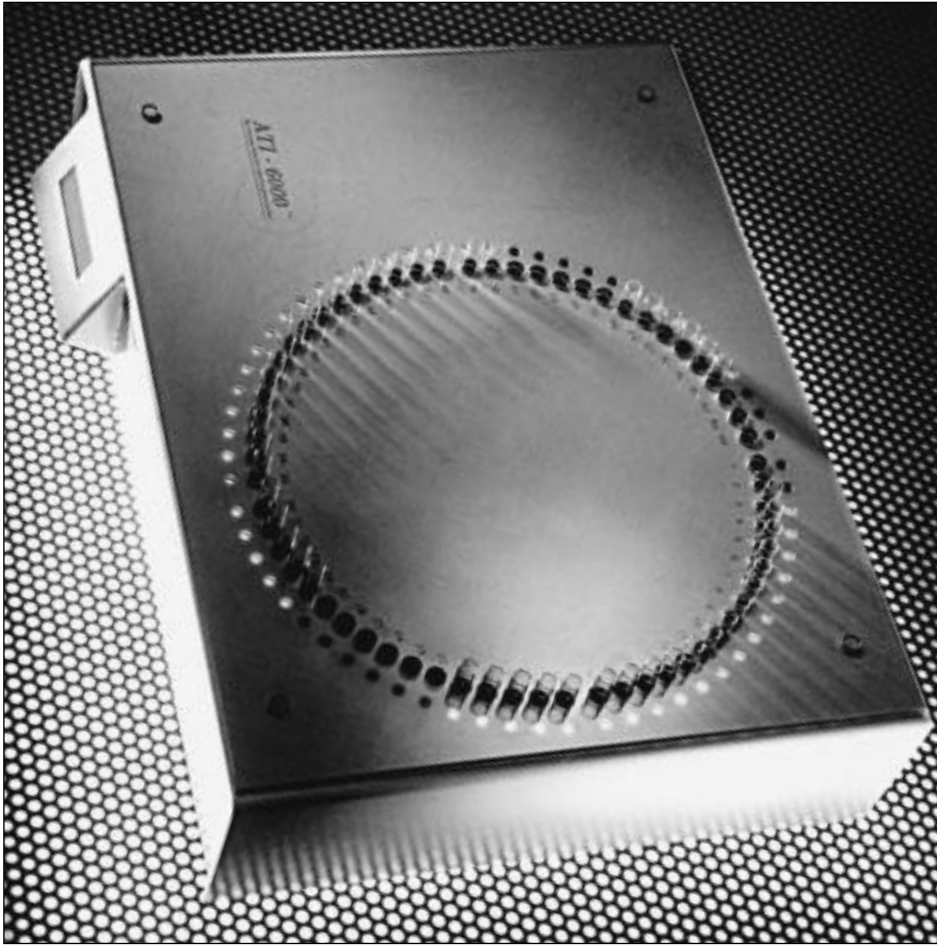
In modern endotoxin analysis, an extract (Limulus Amebocyte Lysate, LAL) derived from the blood cells of the horseshoe crab, *limulus polyphemus*, becomes turbid and clots in the presence of bacterial endotoxins. The endotoxins are released by gram-negative bacteria in aqueous environments and are by far the most common and significant pyrogens (fever-inducing agents). It is extremely important that these agents are not present in drugs or medical devices.

The procedure adopted by the ATi-6000 uses an optical transmission "end-point." The endotoxins are quantified by a kinetic-turbidimetric assay of samples to which a specified amount of LAL is added. Higher concentrations of endotoxin cause the turbidity to

increase (and the optical transmission to decrease) more quickly with time – it is this rate of change that is used in the endotoxin assay. LabVIEW analyses the data and determines the time taken for the optical absorption to reach a fixed threshold level. This time, called the onset time, decreases with higher endotoxin concentrations in the sample. The log of the endotoxin concentration is inversely proportional to the log of the onset time. Endotoxin concentrations are quantified using calibration curves generated using known quantities of standard endotoxins.

Before the development of methods based on the LAL reagent, the most widely used method of testing for endotoxins was to inject the test solution into the blood of live rabbits and wait, over a period of several days, for symptoms of fever or shock. Clearly this technique was very slow, inefficient and, given the current controversy over animal testing, undesirable.

LabVIEW Simplifies Procedures
LabVIEW development focused on simplifying the sample tracking and analysis procedures. With 64 channels; a continu-



The ATi-6000 implements the tests of pharmaceutical products for endotoxins in an efficient manner, enabling high sample throughputs with minimal operator effort.

ous, rolling program; six different categories of samples (unknown sample, standards in water, standards in product, sample spikes, negative controls, and positive controls); and several replicates, the requirements of the software were quite demanding. Because each well has its own separate optical measurement, the user can randomly access the wells, start, stop, and repeat tests at will. The logger software, which communicates via RS-232 with the ATi-6000's onboard microprocessor, simplifies the procedure using an intuitive 64-button carousel menu.

When the user activates a channel button, the user obtains an instant status report for that channel, including the kinetic trace, if a user is analysing a sample. At this point, the user can also read or edit additional information relating to dilution factors, standard ranges, and so on. With the continuous rolling program, the user can insert samples into each well at any time and in any order while online. Using the sample set-up menu, the user configures standards sets, defines units, and enters lot numbers for the various solutions used in the assay.

With the analysis procedures, the user processes data in a variety of ways with minimal interaction. The user can even plot raw kinetic optical density profiles on the screen from data files on the hard disk. The user saves considerable disk space by storing the optical density profiles as seventh-order polynomials in the logging stage and reconstructing them for inspection during the analysis procedure. The user can also select integral calibration curves from the data files and modify them, if necessary, according to a recommended procedure. For example, the user can delete outlier points or even whole concentrations using the mouse.

When the user is satisfied with the calibration curve, which can be archived, then the user can process all the data against the calibration statistics. The user may also choose to analyse a data set against a previously archived calibration. Using the calculate option, the user can view the results, together with hard copies of the results certificate and calibration graph.

LAL testing is now a well established technique for testing pharmaceutical products for endotoxins. The ATi-6000, with the LabVIEW interface, implements the turbidimetric LAL test in an efficient manner, giving users a way to achieve high sample throughputs with minimal effort. ▶

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Atlas Bioscan Ltd. manufactures and sells the ATi-6000 together with a wide range of healthcare products. For more information, contact Atlas Bioscan Ltd., Town Cross Ave., Bognor Regis, West Sussex, PO21 2DR tel: 01243 868640, fax: 01243 824859



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