

Better Automation Critical To Cell Analyzer's Award Winning Design

As in any battle, in mankind's ongoing battle with cancer, the first imperative is to "Know thine enemy." But with cancer, the first challenge is to 'see' the enemy. Cancer research and treatment efforts hinge on identification - at the cell level. Immunicon Corporation, a company in Huntingdon Valley, Pennsylvania, has been developing and commercializing diagnostic and research products for rare cell analysis and molecular research, with an initial focus on cancer.

In June 2006, Immunicon's CellTracks® Analyzer II, won a Silver, 2006 Medical Design Excellence Award. The CellTracks Analyzer II is an automated fluorescence microscope used to count and characterize fluorescently labeled cells that are immunomagnetically selected and aligned. It is used with the CellTracks® AutoPrep® System and specific reagent kit.

A write-up about the 2006 Design For Excellence Award in *IVD Technology* said, "The CellTracks Analyzer (II) was seen as the logical extension of Immunicon's automation program that focuses on low prevalence cancer cells that can be tracked from a blood sample and then characterized with little human intervention." Unlike its predecessor, the CellSpotter® Analyzer, the CellTracks Analyzer II is automated.

Discontinued Components... The Mother Of Invention

In the beginning... Immunicon faced not having a product within a year. Both the manufacturers of an off-the-shelf fluorescent microscope and the digital camera that went on it (which Immunicon had been customizing to create the CellSpotter Analyzer) announced they were discontinuing these products. So, beginning in January 2004, they launched the project to design a replacement.

Setting The Stage

According to Frank Modica, Manager of Mechanical Engineering for Immunicon, who had responsibility for the overall mechanical design, "It all started with how we chose to drive the mechanical stages. Rather than a conventional stepper motor we went with a linear motor. That required us to go back to the drawing board for the stage designs."

They decided to use piezo electric motor technology in conjunction with linear bearings, so that it behaves like a microscope stage under computer control. Art Marlin, the Principal Manufacturing Engineer and Project Manager, remarked that they wanted to be able "To tell the stage where to go within micron resolution."

Achieving Perfect Registration

To understand the challenge the engineers faced, you have to visualize the CellTracks Analyzer II's stages. As Frank Modica describes it, "There are four stages that we use. Two of them position the sample. The third one is the focus stage that positions the

objectives so that the images are in focus. The fourth one moves the proper filters in place, which produces the imaging in the three colors.” The automated movements within the instrument, as depicted by Art Marlin, “work in concert with one another to take multicolored images of the cellular sample that is in the chamber.”

The linear bearings they would choose would have to meet specific requirements in order to achieve perfect positioning. These were determined by the amount of space within the product envelope, distance to be traveled, load to be carried and most critical of all, the degree of accuracy needed. This instrument’s profile or envelope dictated miniature bearings be chosen for their reduced height. At three hundred millimeters, for a medical application, the instrument has a large stage, but it is not high load. However, the alignment and accuracy of the stage was strategic. A cross roller type linear bearing provides the most accurate form of linear motion, so, according to Art Marlin, “The cross roller bearing is in the X coordinate. We needed that to keep the X and Y stationery because any movement between frames could distort the images. We have two, three hundred seventy five millimeter slide guide bearings that are in the long (Y axis) length.”

SVS Cross-Roller Slide Way

The cross roller bearing they chose comes from NB Corporation. It is the SV type slide way that consists of two R type roller cages which have precision rollers in a cross arrangement and four rails having V-shaped raceway surfaces. Rollers provide a larger contact area than ball bearings. That reduces elastic deformation resulting in consistently precise movement. Since the rollers do not recirculate, they are all carrying the load, which produces greater rigidity as well as high load capacity. Another benefit of their not recirculating is less frictional resistance fluctuation. In fact, there is little or no difference between static and dynamic frictional resistances - even under low-load conditions - making them well suited for minute motion. Being all stainless steel makes them ideal for clean room applications.

Art Marlin claims that they have gotten greater positional accuracy. What they are looking at is an overlay of three images of the cell taken in three different colors. So if those images are not registered, one on top of the other, you really do not get an idea of what the cell looks like. He says the registration is greatly improved. The instrument is connected to a PC so the images are seen on the typical flat screen PC monitor. The system magnifies the cell at 10X but, depending on the screen resolution, it can be seen as far larger.

Precise Miniature Slide Guides

For the three remaining axes, Immunicon chose NB’s SEB type slide guide, which consists of a block and a guide rail, both of which have two precision ground raceway grooves. The two-raceway and four-point contact structure of the SEB types minimize their height making them well suited to installations with limited space. Being relatively wide, the SEBS provide greater moment load - more than the project actually required. More importantly, the SEBS standard radial clearance is twice as accurate as conventional slide guides. The economical nonretained-ball version provides friction-free short travel distances in both single and double widths - both of which were used in the Analyzer.

Time And Cost Constraints

As Frank Modica explains, “We had a very rapid development cycle for this. Being able to go through a few design iterations and having the material was important. The quality had to be there but the delivery was key in getting this done in the time allotted. One of the major competitors wanted six to eight weeks to get product from Japan. NB was able to deliver, typically, in three weeks. The NB bearings had the performance we needed plus the price was very attractive. Cost was a factor.”

There are five NB bearings used - one in each of the first three stages and two in the fourth stage. John Badiali of NB, saw the validity of the application and assisted Immunicon from its inception in January, 2004 to production release in June of 2005. Frank Modica attests that, “There have been no performance problems. It has been performing excellently.” He gives credit to NB for being, “Very responsive to our needs.” Art Marlin feels that, “John helped us to achieve getting the prototype components through their office within a short period of time, which helped us expedite evaluation of system components. The bearings performed smoothly and were able to give us the necessary cell resolution in the detail that we need for analysis.”

Crises Averted - The Search For One Cell In A Billion Goes On

The importance of the CellTracks Analyzer II is better understood as part of a complete process. Cancer metastasis occurs when cells (Malignant carcinomas are derived from epithelial cells that are not normally found in circulation.) shed from the primary tumor enter the circulation and begin to grow in distant locations of the body. The scientific challenge is to develop a method to capture very small numbers of these circulating tumor cells (CTC) from a background of billions of cells in a tube of blood. Immunicon uses a 'systems' approach. Their CellSave® Preservative Tube was developed to preserve the fragile CTCs during their trip to the lab site. The CellTracks AutoPrep System standardizes and automates sample preparation. Reagents were developed for the CellSearch™ System, marketed by Veridex, LLC, a Johnson & Johnson company, to optimize recovery of CTCs. The CellTracks Analyzer II is used to count and characterize CTCs. So you can understand Immunicon’s satisfaction at bringing a better, award-winning, product to market in time to continue facilitating, without interruption, important cancer research and diagnostic work. (1,541 words)

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