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AATI Rides the Next-Gen Sequencing Wave

Firm Is Positioned to Meet Rising Demand for Automated Nucleic Acid Analysis

Gail Dutton

Advanced Analytical Technologies, Inc. (AATI) is using the boom in next-generation sequencing and interest from emerging markets to help drive its capillary electrophoresis instrumentation business. "Next-gen sequencing for DNA is growing by leaps and bounds in the United States and European Union, with strong growth in Asia," notes Steve Siembieda, AATI's COO. Siembieda is seeing an uptick in South America, too, as well as increasing interest in RNA sequencing: "Next-gen sequencing for RNA analysis is exploding."

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Advanced Analytical's Fragment Analyzer is a fluorescence-based capillary electrophoresis instrument for both sizing and quantifying nucleic acids (DNA and RNA). By using an intercalating dye coupled with an LED light source, the instrument can do without fluorescent-labeled primers while separating dsDNA fragments and RNA (mRNA and total RNA).

Siembieda also sees solid growth potential in emerging markets, where researchers are just becoming involved in sequencing. "South America and Asia, with the exception of Japan and the Beijing Genomics Institute in China, are about 15 years behind the United States and European Union in terms of sequencing technologies," Siembieda observes.

For AATI, these trends create market opportunities well matched with its technology platform. AATI boasts a wide customer base, and the company's instrument design, asserts Siembieda, "lets us work effectively across the spectrum of markets." For example, AATI's technology platform can help researchers involved with next-gen DNA and RNA sequencing, population genetics, and genotyping.

A Key Decision

AATI was formed in Ames, IA, in 1998. In 2006, AATI merged with CombiSep, also in Ames. "This merger was remarkable," states Siembeida, "because it brought together two completely different thought processes, bringing symmetry to the two groups." Originally, AATI was focused on flow cytometry, but leading up to the merger, the company decided that the molecular market could benefit from CombiSep's core technology—capillary electrophoresis.

CombiSep's solutions enabled researchers to analyze up to 96 samples in parallel by capillary electrophoresis with UV absorbance detection. In 2010, AATI licensed the flow cytometry platform to Becton, Dickinson and Company and refocused its efforts on capillary electrophoresis.

"We were the first company to develop a method for analyzing both quality and quantity of genomic DNA," recalls Siembieda. This initiative was taken about two years ago, when AATI combined quality and quantity measurements into one automated step.

Competitive Advantages

"We can take on large fragments of DNA, separate them, and then detect quantity," adds Siembieda. "In the past, researchers had to run agarose gels to assess nucleic acid quality and, in a separate step, measure quantity with a spectrophotometer or fluorimeter."

AATI's technology platform "…uses a dye that integrates into the DNA sequence nonspecifically, excites it with fluorescent light, and records the emissions with a CCD camera. This is better than fluorescence alone because this method separates fragments, allowing them to be measured," Siembieda explains.

AATI's other key competitive advantage is its ability to perform the longest reads in the industry, making it easier to assemble genome sequences. "We resolve fragments from a low of 2 base pairs up to 40,000 base pairs," says Siembieda. "Our competitors focused on small fragments. We did that, but also recognized we could analyze longer fragments and size them accurately." AATI's notable users include the Dana Farber Cancer Institute, the Institut Pasteur in France, the TATAA Biocenter in Sweden, and the RIKEN Institute in Japan.

"There's a misperception about our instruments," Siembieda admits. "Because they have many drawers, people think they're high-throughput instruments. Competing instruments analyze samples one at a time, while our instruments can look at 12 or 96 samples in parallel." This multiplexing, combined with the ability of the operator to load up to three 96-well plates and then walk away, results in improved workflow. "We engineered flexibility into the platform so it can grow as the research needs change, using the same instrument body.

New Challenges

"We haven't exhausted the applications possible for our instruments," adds Siembieda, who is contemplating applications beyond DNA analysis. "We know there are other molecules that need to be analyzed and other applications that could become more efficient."

One potential application is the analysis of the hundreds of millions of fixed formalin paraffin-embedded (FFPE) tissue samples in hospitals and research centers. "Sequencing those will provide a lot of information in short order, with higher throughput than agarose gels and lower costs than lab-on-a-chip-based technologies," explains Siembieda. "FFPE samples are finite and not replenishable, so labs want to use as little sample as possible when analyzing them, which is possible with the high sensitivity of AATI's capillary electrophoresis technology."

To address some of these emerging applications, AATI is launching a new instrument at the end of the first quarter that improves the workflow for manual agarose electrophoresis. "Medical personnel may run a dozen 96-well plates per day using agarose electrophoresis," observes Siembieda. "Traditional capillary electrophoresis, however, isn't fast enough or accurate enough. We're successful because we're running parallel capillary electrophoresis."

Recently, AATI added a new instrument, the Fragment Analyzer™, which incorporates fluorescence detection to analyze the quantity and quality of nucleic acids for next-gen sequencing, genotyping, checking RNA quality and quantity, and working with microsatellites (also known as simple sequence repeats, or SSRs).

Advanced Analytical Technologies

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Focus: AATI develops capillary electrophoresis solutions to improve sample handling and workflow to accelerate research in pharmaceutical, life science, and biotechnology laboratories.