Advanced Analytical Touts Fragment Analyzer's Versatility, Automation to NGS Users

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By Julia Karow

About half a year after introducing a new capillary electrophoresis instrument for analyzing DNA and RNA fragments, Advanced Analytical is seeing good demand for the system from next-generation sequencing users aiming to streamline their library preparation process and has sold about 85 instruments so far.

Last month, the company said that in order to accommodate demand for the instrument, called Fragment Analyzer, it has increased its production capacity by more than 50 percent and has increased its staff by five since January, with plans to add another 10 to 20 employees in the near future.

In addition, Advanced Analytical is looking into developing a high-capacity preparative instrument for the isolation of DNA fragments of defined length for next-gen sequencing applications.

Founded in 1998 and based in Ames, Iowa, the privately held firm provides a variety of CE-based instruments for applications such as oligonucleotide purity analysis, acid dissociation constant measurements, protein separation, DNA genotyping, and nucleic acid fragment size and quality analysis. The company has a European office and laboratory in Heidelberg, Germany, and sells its products through distributors in other parts of the world.

At the Advances in Genome Biology and Technology meeting in Marco Island, Fla., in February, Steve Siembieda, Advanced Analytical’s chief operating officer, provided an overview of the Fragment Analyzer, an automated CE instrument the company released about six months ago, and its applications in next-gen sequencing library prep.

Siembieda told In Sequence that so far the company has sold about 85 Fragment Analyzer systems, which have a list price of $36,000. While not all of those instruments have been installed yet, he estimated that close to half of them will be used to analyze the size and quantity of DNA fragments that go into next-gen sequencing libraries. Many NGS users are academic customers at the moment and comprise both low- and high-throughput users.

For NGS applications, the system competes with other analytical DNA sizing systems, such as the Agilent 2100 Bioanalyzer, which Siembieda said is less expensive; the Agilent 2200
TapeStation System, which he said costs about the same; Caliper's LabChip GX, which he said is more expensive; and Qiagen's QIAxcel System.

The Fragment Analyzer uses a set of either 12 or 96 capillaries to separate DNA or RNA in order to determine their size and quantity. The company claims that it offers the greatest sensitivity, the highest resolution over a wide range of sizes, and the fastest separation times of all instruments currently on the market.

Besides next-gen sequencing fragment analysis, applications for the instrument include the analysis of microsatellites, genomic DNA, total RNA or mRNA, plasmids, and large PCR amplicons, as well as mutation detection.

The firm sells a next-gen sequencing fragment analysis kit for 500 samples and a size range from 35 bases to 6 kilobases. According to Siembieda, the analysis costs about $1.50 per sample.

Compared to other systems, an important benefit for next-gen sequencing users is that most of the Fragment Analyzer’s workflow is automated, he said. Users can load the instrument with up to three 96-well plates, which are analyzed sequentially. The instrument automatically fills the capillaries, loads the samples, and starts the run. A run takes about 45 minutes, which Siembieda said is fast compared to other instruments.

Because its capillaries are up to 80 cm long, the Fragment Analyzer can also resolve larger fragments than other systems — up to 40 kilobases in size — and achieves better resolution, he said. Though many types of next-gen sequencing libraries do not require fragments that large, this feature is important for libraries for the PacBio RS and mate-pair libraries for the 454. Also, nanopore-based sequencing systems currently in development might require libraries with long DNA fragments, he added.

"It is clear that sequencing is moving to larger fragments," Siembieda said. "People want bigger fragments for easier assembly."

The Fragment Analyzer can also load the capillaries with two different types of gels that are stored on the instrument, so users can switch from one application to another without having to change gels manually.

Besides sizing DNA fragments, NGS customers can use the instrument to check both the quantity and quality of genomic DNA, so they require no additional instrument for that, he noted.

The Genetics Diagnostic Laboratory at Children's Hospital Boston installed the Fragment Analyzer last fall after looking into several options. It has been using the instrument to assess the quality of sequencing libraries for its Ion Torrent PGM as well as to analyze the quality of genomic DNA after extraction.
Hal Schneider, clinical laboratory manager of the Genetics Diagnostic Lab, especially values the versatility of the instrument. "We can basically put a plate on and use it for lots of other things" besides sizing DNA fragments, he said. "Just in general, we are looking to use it to replace any gels in our lab," he added.

Schneider said he also likes that the DNA dye used by the instrument is double-strand specific "so you are getting a really good quantification if you set up your markers correctly."

His lab currently has the 12-channel version but is thinking about switching to the 96-channel version to accommodate its growing throughput.

Schneider previously used Agilent's Bioanalyzer to check the quality of NGS libraries, and looked into getting the Agilent TapeStation. Both instruments are "good also, there is nothing wrong with them," he said. However, for those preparing large numbers of sequencing libraries, "you make your life much easier using the Fragment Analyzer," he said.

Advanced Analytical is also currently looking into developing a preparative instrument for next-gen sequencing, which has been requested by many of its customers, Siembieda said. The goal is to launch that system, which will have a large capacity, about a year from now.

It will likely compete with existing preparative instruments, for example Sage Science's Pippin Prep and BluePippin, and Caliper's LabChip XT.