

A new level of productivity in high-resolution proteomics

AB Applied
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Applied Biosystems

4700

Proteomics Analyzer



productivity x Delivering on the promise of proteomics

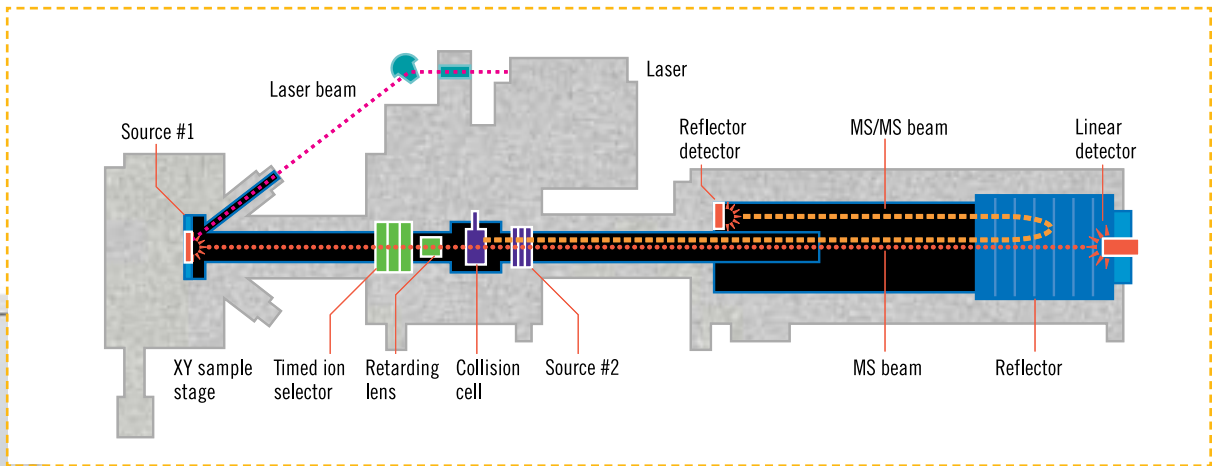
Introducing the Applied Biosystems 4700 Proteomics Analyzer with TOF/TOF™ Optics, the first analyzer to provide the power and performance needed for high-resolution proteomics.



In 1997, Applied Biosystems introduced technology that advanced DNA sequencing and hastened the first draft of the human genome, ushering in new discoveries of genetic sources of disease and potential drug targets.

But the genomic revolution is only the first step in fully understanding the biology, diagnosis, and treatment of diseases. Although proteomics holds enormous promise, protein identification and characterization pose far more complex and time-consuming problems — unless proteomics research can be advanced and integrated with greater speed, efficiency, accuracy, and resolution.

power = 4700



The TOF/TOF™ optics acquires data in linear and reflector MS and true precursor-selected MS/MS modes. This patented technology provides rapid protein identification and extensive characterization by coupling MALDI throughput and ease-of-use with MS/MS specificity.

With its capacity for unprecedented productivity, the Applied Biosystems 4700 Proteomics Analyzer provides significant biological information at speeds of up to 1,000 samples per hour.

Applied Biosystems Proteomics: experience, vision, commitment

Applied Biosystems brings to bear a 20-year history of innovation helping researchers overcome challenges in protein analysis. As part of this commitment, Applied Biosystems established the Proteomics Research Center (PRC) in March 2000. In conjunction with a global network of collaborating laboratories, the PRC develops new approaches to advancing the science and technology that support proteomics by modeling real-world analytical

and bioinformatics problems, validating workflow improvements, and developing innovative solutions to both current and predicted challenges in protein studies.

Building on its legacy of innovation and vision for proteomics, Applied Biosystems delivers a new level of productivity for your high-resolution proteomics endeavors. You can now identify, characterize, and quantify proteins more rapidly than you ever thought possible.

speed x speci Breaking the analysis bottleneck

The Applied Biosystems 4700 Proteomics Analyzer makes it possible for you to increase the speed of sample analysis and expand both the range of possible projects and the amount of biologically significant information generated from complex proteomics samples. This fully automated platform facilitates a better understanding of biology and the biology of disease — all without compromising performance.

High-productivity protein analysis

The Applied Biosystems 4700 Proteomics Analyzer with TOF/TOF™ Optics is the first analyzer designed to meet the scale and scope of the proteomics challenge. The fully automated platform permits the acquisition of information-rich, high-quality MS and MS/MS spectra on a high-throughput, easy-to-use MALDI platform, thereby removing the analysis bottleneck from proteomics experiments.

Multiple workflows

The Applied Biosystems 4700 Proteomics Analyzer is flexible enough to support a wide variety of front-end sample preparation methods, such as 1-D and 2-D gels, multi-dimensional liquid chromatography (MDLC), or Applied Biosystems proprietary Isotope Coded Affinity Tag technology, as well as back-end bioinformatics platforms. This flexibility enhances existing workflows, leveraging your current research investments and enabling you to acquire information that was previously inaccessible. The 4700 Proteomics Analyzer is an automated, high-capacity platform that lets you conduct a broad range of studies to better understand the building blocks of life and disease.

A key differentiator: patented TOF/TOF™ optics

The unique advantages of the 4700 Proteomics Analyzer stem from its coaxial tandem time-of-flight MS/MS configuration. This exclusive Applied Biosystems design provides high-energy collision-induced dissociation for high-quality fragmentation with important structural information such as immonium ions, side-chain cleavages, and internal fragments. With this new level of structural detail, you can elucidate important post-translational modifications and handle challenges like leucine/isoleucine differentiation and other complexities within high-resolution proteomics.

The information-rich, consistent fragmentation patterns allow definitive protein identification and extensive characterization of multiple proteins. The large mass range and high-energy fragmentation of the TOF/TOF™ optics also permit you to analyze proteins without prior digestion, simplifying your protocol. The high rep-rate laser and high-speed data acquisition system provide superior sensitivity and dynamic range for successful analysis of important low-copy proteins like transcription factors and protein kinases. Coupling the throughput and ease-of-use of MALDI with MS/MS specificity yields accurate protein identification and extensive structural information at speeds of up to 1,000 samples per hour.

specificity = 4700



Buck Institute for Age Research

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STUDY: *Haemophilus ducreyi*

is a gram-negative bacterium that causes chancroid, a sexually transmitted disease that is prevalent in many developing countries. In addition to the morbidity directly caused by *H. ducreyi* infection, chancroid facilitates the transmission of HIV.

GOAL: To identify as many *H. ducreyi* proteins as possible using data from the recently completed genome of *H. ducreyi* strain 35000.

WORKFLOW: The researchers analyzed the whole-cell lysate of the bacterium by multi-dimensional LC on the Vision™ Workstation, then followed up with automated MS and MS/MS analysis on the 4700 Proteomics Analyzer. After they generated the MS/MS spectra, they performed an automatic Mascot™ database search to identify the proteins.

RESULTS: Compared to a 2-D gel approach, the MDLC workflow performed above identified substantially more proteins with 90% less starting material. The researchers obtained MS data on 114 MALDI sample spots from one ion-exchange fraction in less than 4 minutes, and MS/MS data on 624 precursor ions contained in these samples in less than 2 hours, including search time. 190 unique proteins were identified from the MS/MS spectra. Each of the other 19 ion-exchange fractions yielded more than 500 precursor ions per fraction for automated MS/MS acquisition. Using the genome of *H. ducreyi*, 500 MS/MS Mascot searches were completed in 4 seconds.

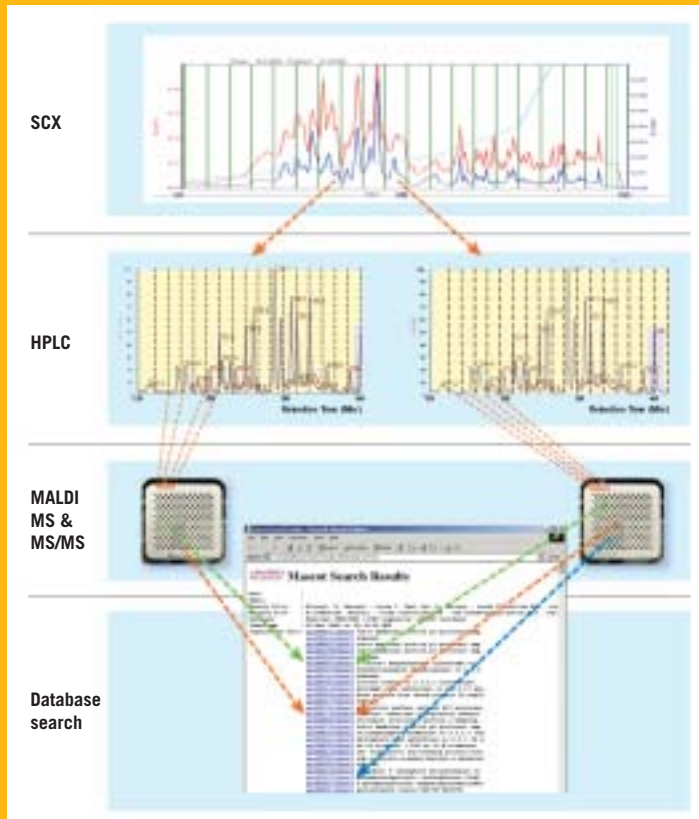


Figure 1. MDLC workflow utilizing the sensitivity and specificity of MALDI MS/MS identifies 190 unique proteins from a single ion exchange fraction in 2 hours.

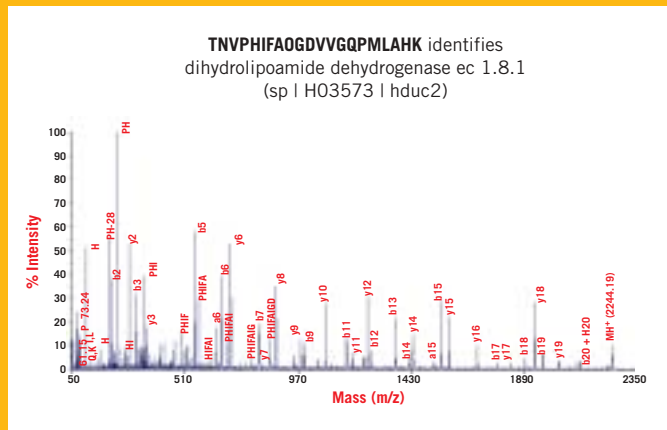


Figure 2. MALDI MS/MS of 2244 Da precursor. The TOF/TOF™ optics provides excellent sequence coverage and superb resolution across the entire mass range for greater mass accuracy and superior confidence in protein identification.

IMPACT: High-throughput with great sensitivity leads to rapid, accurate progress in high-resolution proteomics, expanding basic biological knowledge.

sensitivity x ac Digging deeper into the proteome

Ease-of-use, sensitivity, accuracy, speed, and throughput — all essential for your success in high-resolution proteome analysis and systems biology. The Applied Biosystems 4700 Proteomics Analyzer can shift your research from time-consuming analysis of individual proteins to studying complex biological systems that let you discover and understand the relationships in the protein complement down to minute differences.

No-compromise protein analysis

Before the introduction of the Applied Biosystems 4700 Proteomics Analyzer, researchers had to compromise speed, sensitivity, accuracy, ease-of-use, or depth of analysis. No longer. The 4700 Proteomics Analyzer sets the standard for future high-productivity protein discovery. Thanks to its TOF/TOF™ optics, the 4700 Proteomics Analyzer rapidly delivers high-resolution proteomics data of unprecedented quality. Using these results, researchers can confidently mine databases, translate accurate molecular weight data into enhanced structural information, and automatically generate protein expression analysis. The 4700 Proteomics Analyzer gives you highly reliable results to advance your complex biological research.

MALDI-MS integration for superior performance and ease-of-use

Unlike LC/MS systems, where the analytes are transient, eluting in a limited period, the static sample configuration of the MALDI format in the 4700 Proteomics Analyzer permits richer, deeper analyses and more information per analysis. Add to this true MS/MS capability, and the 4700 Proteomics Analyzer easily detects details that a single pass of MS or MS/MS analysis might miss.

By combining ease-of-use, sensitivity, accuracy, and speed, the Applied Biosystems 4700 Proteomics Analyzer represents a compelling new solution for any industrial or academic laboratory that seeks to optimize its protein expression analysis including identification and characterization of proteins.

The 4700 Proteomics Analyzer is already in use at several labs around the world, conducting basic biological studies to elucidate pathways, differentiating between normal and abnormal cell samples, and identifying and validating potential drug targets. It can shift the research burden from the time-consuming task of analyzing individual proteins to doing high-resolution proteome analysis and complex systems biology. The Applied Biosystems 4700 Proteomics Analyzer can speed biological research and the development of new drugs and diagnostics without sacrificing quality of results.

Accuracy = 4700



**Lund University,
Lund Sweden**

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STUDY: Characterize nuclear proteins in human primary fibroblast cells.

GOAL: To link proteins expressed in fibroblast cell nuclei to a phenotypic switch in order to understand the molecular basis of fibrosis seen in asthma patients.

WORKFLOW: Researchers used 10 million cells to generate 1–2 million purified cell nuclei. They isolated fibroblast nuclei before and after activation by TGF-β. They then employed high-resolution 1-D and 2-D gels and silver-stained gel image analysis to select spots of interest. They identified the proteins on the 4700 Proteomics Analyzer with protein mass fingerprint analysis, followed by MS/MS sequence tag analysis.

RESULTS: From very limited starting material, researchers identified 380 nuclear associated proteins using MALDI PMF combined with MS/MS on the 4700 Proteomics Analyzer. The following protein classes were found:

- DNA/RNA binding proteins
- Enhancer/repressor proteins
- Histones
- Splicing factors
- Structural proteins
- Miscellaneous proteins with known function
- Proteins with unknown function

Approximately 15% of the identified proteins have yet unknown functions. With the protein identifications available researchers plan additional experiments to further validate their nuclear localization and to study their differential expression under the conditions of the activation of fibroblast cells by TGF-β.

(This research has been submitted for publication.)

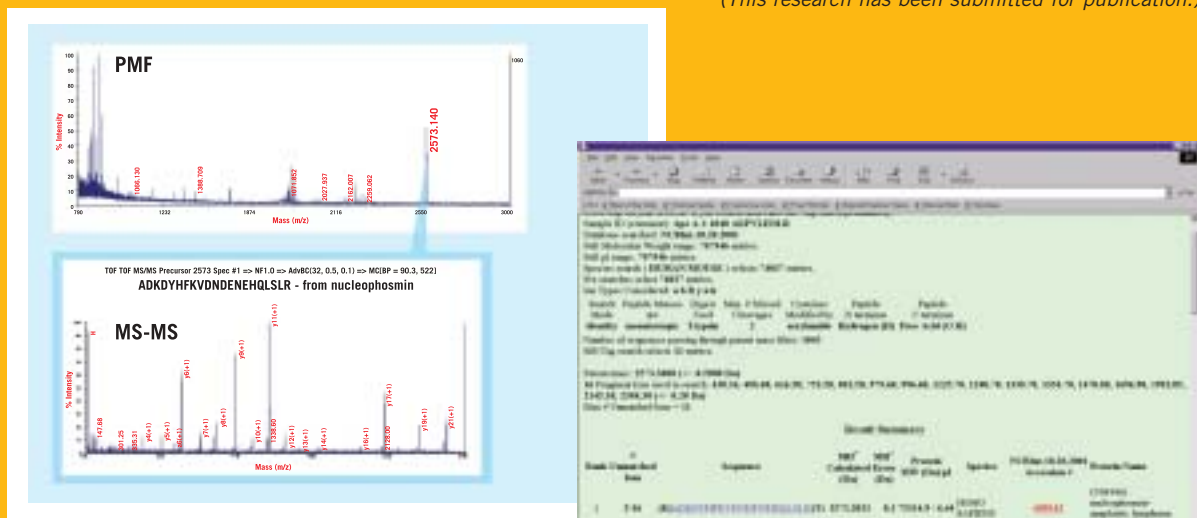


Figure 1. Peptide mass fingerprints from low sample amounts often yield ambiguous database search results. Mascot™ tools combine the PMF data with the MS/MS data on the 2573 Da precursor to identify nucleophosmin with high confidence.

IMPACT: Rapid, concise workflow reveals key proteins associated with the fibrosis seen in asthma patients. Sensitive and accurate protein analysis advances the biological insight of fibrosis and quickly designates steps for further research.

Work at the forefront of systems biology

Proteomics is the new focus in drug discovery and competition is intensifying. The Applied Biosystems 4700 Proteomics Analyzer is a new kind of platform for a new kind of proteomics research, one that demands depth and breadth of protein information at great speed with uncompromising quality.

The 4700 Proteomics Analyzer runs unattended for 24x7 operation, allowing you to focus on results that produce discoveries. Front-end and back-end flexibility ensure that you can conduct a variety of experiments to meet your specific needs. Applied Biosystems backs the performance of the 4700 Proteomics Analyzer with its vast commitment to research in proteomics, its global sales and service network, and the vision that makes us the leading innovator in proteomics.



See the Applied Biosystems 4700 Proteomics Analyzer in action at the Proteomics Research Center (PRC) in Framingham, Massachusetts. Learn more about the PRC and its advanced technologies by taking a virtual tour of the lab at www.appliedbiosystems.com/apps/proteomics.



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