

The Evolution of the Revolution

Applied Biosystems Celebrates 20-Year Legacy of Life Science Innovation

When Watson and Crick announced in 1953 that they had discovered “the secret of life,” they launched a life science revolution that continues to change the practice of modern medicine. Their discovery of the structure of deoxyribonucleic acid (DNA), one of the greatest scientific milestones of all time, enabled researchers to begin elucidating DNA’s protein-making machinery in the cell. Many embarked on finding genes, understanding their protein products, and unraveling the underlying causes and cures of disease. This launched a genetic gold rush, and in 1981 Applied Biosystems was founded to provide the “picks and shovels.”

A Timeline of Applied Biosystems Major Contributions to Life Sciences

Since the company’s founding more than 20 years ago, Applied Biosystems along with its joint ventures, mergers, and acquisitions, has introduced a series of innovative technologies that became cornerstones for modern life science research and catalysts in the life science revolution.

1982 — Protein sequencer opens new avenues for protein exploration — Applied Biosystems first product, an automated gas phase protein sequencer, transforms protein science almost overnight. It was previously so difficult that only about 200 scientists worldwide could successfully sequence proteins. And, at the rate of about ten amino acids per day, it would take months, even years, to elucidate the primary structure of a single protein. The Applied Biosystems 470A Protein Sequencer, a miniaturized bench-top system with robust chemistry, made protein sequencing faster, better, and 1,000 times more sensitive than before.

1983 — DNA synthesis makes primers and probes readily available for first time —

Applied Biosystems introduces the first successful automated DNA synthesizer, making primers and probes readily available to all life scientists for the first time. Previously, synthetic DNA was made by manual methods that were extremely slow and tedious. Availability of the company’s DNA synthesis technology spurred a quantum leap in the number and types of experiments that researchers could perform. It also proved essential to the development of future technologies, including DNA sequencing, and for the polymerase chain reaction (PCR) process, which makes copies of DNA.

1984 — Peptide synthesis becomes new tool to investigate protein function — Applied Biosystems introduces an instrument-reagent system for synthesizing peptides (short protein fragments) that enables researchers to study protein structure and how it relates to protein function.

1986 — Automated DNA sequencing technology sparks the genomics revolution — Applied Biosystems commercializes the first automated DNA sequencer that essentially supplanted the manual, radioactive process that left data in radiograms storable in file cabinets. The system’s automation and its ability to digitize data had an enormous impact on the life sciences by accelerating research and setting the stage for computerized analysis, genome sequencing, database development and bioinformatics, and industries based on these technologies.

1986 — New mass spectrometry technology advances pharmaceutical development —

The joint venture now called Applied Biosystems/MDS SCIEX formed in 1986 focuses on the development of liquid-chromatography/mass spectrometry technology (LC/MS) that enables analysis of biological samples. This LC/MS and subsequent development of LC/MS/MS technology becomes the method of choice for pharmacokinetic applications that determine the course and life of the drug and its metabolites in different fluids and tissues of the body.

1987 — Commercial PCR systems make this new technique widely accessible —

PCR (polymerase chain reaction) becomes a broadly accessible tool for the first time with the development of the first commercial PCR enzyme and thermal cycler instrument. PCR—a chemical process that makes copies of DNA and RNA—is now a basic tool in life science research. The Perkin-Elmer Cetus joint venture developed these initial PCR technologies. Applied Biosystems became owner of this technology as well as the exclusive license from Roche Molecular Systems to develop and market PCR for life science research when it merged with The Perkin-Elmer Corporation in 1993.

1988 — Management of laboratory information becomes high tech — To help laboratories manage the tremendous volume of information generated by new analysis tools, Applied Biosystems introduces the first version of its laboratory information management software (LIMS), a complete system able to manage sample tracking, laboratory processes, workflow, data access and storage information, and assist with regulatory compliance. Today, more than 1,000 laboratories rely on this software, including 17 of the 20 largest global pharmaceutical manufacturers. Applied Biosystems acquired this technology when it merged with the Perkin-Elmer Corporation in 1993.

1990 — Advances in mass spectrometry enhance protein identification and characterization —

Applied Biosystems introduces the first commercial Time-of-Flight (TOF) mass spectrometer with matrix-assisted laser desorption/ionization (MALDI). Subsequent advancements in MALDI-TOF mass spectrometry technology have made it one of the most important bio research techniques for understanding proteins, peptides, carbohydrates, polymers, and other large molecules. Applied Biosystems gained this technology when it acquired PerSeptive Biosystems in 1997.

1994 — Genetic analysis techniques advance the science of human identification —

Applied Biosystems introduces the dot-blot strip for human identification. This DNA-based kit, developed by Roche Molecular Systems and marketed by Applied Biosystems, made

it significantly easier for forensic scientists to employ DNA-based technology. Applied Biosystems advanced the technology further with a succession of kits (based on fluorescent detection of STRs—short tandem repeats) that significantly improve discrimination and sensitivity. Applied Biosystems genetic analysis systems subsequently automated the process. DNA can often be the ultimate proof of identity—for evidence of guilt or innocence in criminal investigations, or identification of victims of catastrophes.

1995 — Real-time PCR enables quantitative gene expression and large-scale genotyping —

Applied Biosystems pioneers real-time PCR instruments and reagents that make quantitative gene expression and high-throughput genotyping studies possible. Real-time PCR allows repetitive testing on many different DNA samples. Typically used in population studies to validate the occurrence of gene mutation or single nucleotide polymorphisms (SNPs) involved in disease or to quantitate the expression level of a disease gene, this technology enables researchers to make advances in basic and human disease research, as well as in drug development and clinical studies. Quantitation for gene expression studies is a revolutionary capability.

1995 — DNA analysis moves into animal parentage and GMO crop analysis — Applied Biosystems introduces PCR-based kits and systems to verify the parentage of livestock and domestic animals, as well as kits for the detection of genetically modified organisms (GMOs) in food, expanding the applications for genetic analysis to agriculture.

1997 — DNA identification detects harmful organisms faster, more reliably — Applied Biosystems employs its core technologies in real-time PCR for the identification of microbes such as Salmonella and E. coli in food and the environment. These DNA-based analyses offer faster, more accurate results for food and water safety, pharmaceutical sterility control, efficient disease outbreak tracking, and the detection of virulent bacterial strains. These tests can often provide same-day results for hundreds of samples, compared with conventional culture methods that require days or weeks.

1998 — Production-scale DNA analyzer enables milestone genome projects —

Applied Biosystems introduces the first production-scale system for DNA sequencing and genotyping—the 96-capillary ABI PRISM® 3700 DNA Analyzer. This powerful system can sequence approximately 900,000 bases per 24 hours with unattended operation. It becomes the

primary technology used to sequence the human genome, enabling the project to be completed years ahead of schedule. This historic milestone, made possible using the 3700 system, was later celebrated at a White House event in June 2000, hosted by President Clinton.

2000 — Customized integration of life science laboratories with professional services —

Applied Biosystems offers Rapid Integration Solutions (RIS)—a world-class professional service to integrate and automate the life science laboratory. This program combines state-of-the-art software products to track and manage samples, robots, instruments, and data for a range of applications including high-throughput genotyping, proteomics, gene expression, high-throughput sequencing, pre-clinical testing, and forensics.

2001 — Mass spectrometry expands capabilities in proteomics and drug development —

Applied Biosystems along with Applied Biosystems/MDS SCIEX have made almost annual advancements in mass spectrometry and its ionization technology. By 2001, these systems provide the identification and characterization of a broader range of small molecules, pharmaceuticals, and biomolecules, including proteins. Scientists now can choose from systems that provide high performance, definitive protein identification with database searching and characterization of proteins, as well as high throughput protein identification expression profiling. These systems have led to an increased understanding of biology and disease as well as the development of new pharmaceuticals.

2002 — Applied Biosystems begins marketing and distributing Celera Discovery System™ —

Applied Biosystems obtains the exclusive marketing rights to the Celera Discovery System™ (CDS), a subscription-based, online discovery platform containing the most comprehensive and current set of curated biological data available, and begins integrating it with the company's other products and services, such as its Assays-on-Demand™ products, to expand the availability and application of genomic data to scientific discovery.

2002 — Genome-wide assay sets provide scientists ready access to the human genome —

Applied Biosystems introduces its Assays-on-Demand™ Gene Expression and SNP Genotyping Products, comprising the most comprehensive collection of functionally validated, ready-to-use assays ever produced. These assays were developed using data from both the public projects and proprietary data from Celera Genomics. The new assay products eliminate the time and costs associated with designing and validating assays,

and enable new, highly productive workflows that significantly shorten the time from experimental hypotheses to results.

2002 — DNA sequencing production rises to a new level —

Applied Biosystems introduces the Applied Biosystems 3730x/ DNA Analyzer, an advanced system that improves data quality and heralds a new level of throughput by sequencing up to two million base pairs of DNA per day. This effectively doubles researchers' production capacity, while dramatically reducing the cost per analysis at a time when genome projects increase.

2002 — Next-generation mass spectrometers further improves accuracy of protein identification and characterization —

Applied Biosystems/MDS SCIEX QTRAP™ LC/MS/MS and QSTAR® XL LC/MS/MS Systems increase speed and provide even higher performance for protein and peptide identification and analysis of small molecule drug metabolites important in therapeutics.

2003 — Stay tuned for new developments from Applied Biosystems —

With major advances in technology and the increasing availability of high-quality biological data, Applied Biosystems is extending beyond instrumentation, reagents, and single applications to integrated genomic and proteomic products, services, and data. The company's goal is to automate workflows for higher levels of efficiency and production, and to link information with experiments so that research results can be intelligently applied to the discovery process. Moreover, life scientists will be able to explore more complex questions, obtain answers faster, and reduce project costs through the integration of information, tools, and assays.

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