Ancillaries and Analyzers

Balances, pH meters, and more were critical to the rise of chemistry.

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Instruments are at the core of scientific discovery; their use has extended the frontiers of science. But it is not just the critical spectrometers and chromatography systems that make science possible. A host of other instruments is necessary for modern science to move forward. Notable among these are the ultracentrifuge, the pH meter, the distiller, the balance, and the tools of X-ray crystallography.

The Centrifuge, Round and Round

Centrifugation, having been around since the mid-1800s, is one of the oldest and one of the most widely used techniques for sample preparation. The ultracentrifuge, devised in the 1920s by Swedish colloid chemist Theodor Svedberg, quickly became one of the most powerful techniques for purification and characterization of biological molecules. In 1923, after constructing various prototypes and refining the design, Svedberg built an instrument that produced 7000*g* of centrifugal force, and he called it the "ultracentrifuge."

In the 1930s, University of Virginia optical physicist Jesse W. Beams further developed the centrifuge, determining the best materials and shapes for rotors and designs for fast drives. Edward G. Pickels, his student, modified the ultracentrifugation technique to make it more reliable and easy to use. He developed the analytical centrifuge for determining particle sizes and the preparative centrifuge for concentrating viruses.

In the late 1930s, Beams marketed the vacuum ultracentrifuge; however, it was not successful. Svedberg also marketed his own instrument, but because of its immense cost, on the order of $20,000 (in contemporary dollars), his commercial endeavor also was not successful. In 1946, Pickels cofounded Spinco (Specialized Instruments Corp.) and marketed an ultracentrifuge based on his design. Pickels, however, considered his design to be complicated and developed a more "foolproof" version. But even with the enhanced design, sales of the technology remained low, and Spinco almost went bankrupt. The company survived and was the first to commercially manufacture ultracentrifuges, in 1947. In 1949, Spinco introduced the Model L, the first preparative ultracentrifuge to reach a maximum speed of 40,000 rpm. In 1954, Beckman Coulter purchased the company, forming the basis of its Spinco centrifuge division.

Today, instruments are manufactured from aluminum alloys and titanium, whereas Svedberg's group used high-tensile steel. Several improvements over the years, including high-speed motors, methods to reduce friction, and development of vacuum systems, have led to modern ultracentrifuges. Larger-capacity units for high-speed centrifugation were critical, and nearly 50 years ago, the International Equipment Co. (IEC) introduced the first large-capacity 20,000-rpm centrifuge.

Today, high-speed centrifuges, rotors, and supplies are provided by companies such as Beckman Coulter, Kendro/Sorvall, and Thermo IEC. Other companies offer equipment and supplies to expand the utility of centrifugation, including Brinkmann Instruments, Corning, Millipore, and Whatman.

Coupled to the developments in electron microscopy, which enable researchers to see organelles they are separating by ultracentrifugation, advances in the ability to formulate structure-function relationships have been profound. And the development of the first microcentrifuge (microfuge) by Beckman Coulter has made possible some of the most important advances in genomics through its ability to enhance DNA and RNA separations in small-scale processes.

Many important applications of the ultracentrifuge in the modern laboratory are biological, with the purification and separation of cell components made possible by gradient and other techniques key to advances in biotechnology.

Top: pH meters, Courtesy of Phoenix Electrode Co. (includes original Beckman unit)

Center: Ultracentrifuge ad ca. 1950s, *Made to Measure*, 1999

Above: Mettler analytical balance, courtesy of Mettler Toledo

Power to the pH

The measurement of hydrogen ion concentration, or pH, is widely used in chemistry and biology laboratories and has become an integral part of research. Until the late 1880s, litmus paper was used for the qualitative determination of alkalinity or acidity.

Søren Peter Lauritz Sørensen wrote the classical paper on pH in 1909. Sørensen, a Danish biochemist, suggested a convenient way of expressing acidity—the negative logarithm of hydrogen ion concentration. By 1915, Sørensen and others developed systems that used a hydrogen electrode, although the need for highly purified hydrogen gas made it impractical at the time. Soon, Fritz Haber and Z. Klemensiewicz replaced the hydrogen electrode with a simpler glass electrode, but measurements were time-consuming and expensive. In the 1920s, Leeds and Northrup Co., now a division of Honeywell International, introduced the Bovie hydrogen ion potentiometer. And in 1929, Duncan MacInnes and Malcolm Dole perfected a glass composition for pH electrodes (later known as 015 pH glass from Corning).

In 1934, rapid and inexpensive pH devices became a reality when Glen Joseph asked classmate Arnold O. Beckman, then an assistant professor of chemistry at the California Institute of Technology, for help measuring the acidity of lemon juice. Beckman's "acidmeter" design simplified and expedited acidity and alkalinity measurements. The unit quickly became an indispensable analytical tool. In 1935, Beckman formed National Technical Laboratories (NTL), which developed the first commercial pH meters and was the beginning of Beckman Instruments, now Beckman Coulter.

World War II gave Beckman's business an important boost. Not only did the war force NTL and other companies to increase production, it also introduced the company to a much wider market—in business, engineering, science, and the military. Beckman's expanded line of instruments, and the marketing of its ModelG pH meter (acidimeter) by Arthur H. Thomas Co. of Philadelphia for $195, helped the company grow exponentially as part of the postwar business and science boom. Today, pH meters are a mainstay of many instrument-manufacturing companies, such as Beckman Coulter, Metrohm, Sartorius Corp., and Thermo Electron Corp.

Modern research is especially interested in developing new and better electrodes (for measuring pH as well as other specific chemical species) and microelectrodes for a host of miniaturized and automated processes. Microelectrodes for a variety of purposes are now offered by most companies, including Thermo Orion; companies such as Microelectrodes, for example, provide flow-through microelectrodes and bendable electrodes, and Cole-Parmer offers unbreakable electrodes designed for testing samples as small as 10 µL, capable of fitting into microwell plates or capillary tubes, thereby adapting to the needs of modern biotechnology.

THE SWISS CONNECTION

In 1945, Erhard Mettler launched the single-pan balance. Mettler, a Swiss engineer, started Mettler Instrumente AG, a precision mechanics company in Küsnacht, Switzerland. His modification of the double-pan balance to the single-pan design revolutionized the way analytical beam balances were made. Unlike its dual-pan predecessors, Mettler's balance had only a single fixed weight on the beam's long arm. He invented the substitution principle with which a single-pan balance could be produced in series. With this advance, the single weighing pan gradually replaced conventional two-pan balances in the laboratory.

In 1973, Mettler Instrumente AG introduced the first fully electronic precision balance, the PT1200. Today, electronic balances have replaced Mettler's once-revolutionary single-pan balances. In 1980, Mettler sold his business to Ciba-Geigy AG. And in 1989, the Mettler firm acquired Toledo Scale Corp., the largest U.S. manufacturer of industrial and retail scales. The combination of these two industry leaders gave birth to Mettler Toledo. In 1996, Ciba-Geigy AG sold the company to New York-based AEA Investors.

Distillation

According to archaeologists, distillation, the process of separating a liquid into different parts by evaporation and condensation, began in ancient Egypt and Mesopotamia for medicinal purposes. Indeed, distillation apparatus made from terracotta and dating from about 3000 B.C. has been found.

Early distillation vessels were inefficient, partly because of the escape of vapor. It was not until the late 18th century that water-cooled condensation columns were developed, seemingly independently, by three European researchers. This form of condenser is commonly known as the countercurrent, or Liebig, condenser, and its basic design is still in use today. Early in the 19th century, some chemists were still conducting experiments using ordinary materials such as wineglasses.

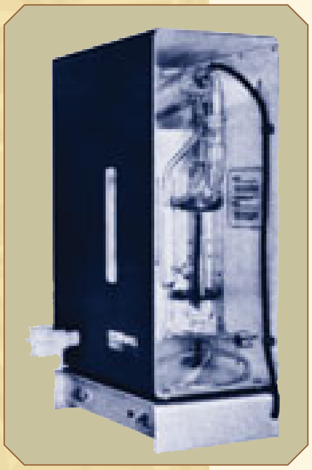
The industrial revolution introduced a shift from small-scale batch operations to large-scale continuous mass production and the development of vacuum distillation methods. In the chemical industry, labor-intensive batch distillation was replaced with continuous distillation, which allowed greater throughput. The introduction of continuous distillation, in turn, greatly reduced the price of gasoline, which powered the machines of industry.

World War I brought an end to German-supplied laboratory and scientific glassware, but manufacturer KimbleGlass (now Kimble/Kontes) filled the void. By the early 1950s, the distillation assembly was greatly improved with the introduction of standard ground glass joints, and with the addition of thermometers, evaporation and pressure could be controlled. In addition, data could be collected automatically. Today, many industries such as petroleum, beverage, chemical processing, and petrochemical still use distillation in critical separations.

Distillation is also probably the oldest technique for purifying water. Although no individual treatment device removes every contaminant from water, with the advent of carbon adsorption, deionization, ultrafiltration, reverse osmosis, ion exchange, and UV irradiation, it is now possible to manufacture not only chemicals but also "pure" water for consumption as well as industrial use. Barnstead International, founded in 1878 in Boston, has long been a major distributor of these types of purification devices. Laboratory Construction Co., now Labconco Corp., founded by Ralph Callaway and Philip Goldfisch in 1925, also distributes purification devices.

The Balance

Balances have been used since 5000 B.C. The earliest surviving chemical balance, developed by Joseph Black in 1754 in Edinburgh, was instrumental in the discovery of carbon dioxide, the first gas to be identified. But Black's design proved problematic. Beams of early balances flexed when loaded; a more rigid balance beam was needed.



Above: Corning Laboratory Products ad, *Analytical Chemistry*, 1968

Around 1820 in London, manufacturer Charles Robinson supplied chemist William Hyde Wollaston with a short-beam balance. Its perforated triangular design allowed the balance to be adjusted at each end of the beam. In 1870, the industrial processing of aluminum developed by chemist Friedrich Wöhler enabled Florenz Sartorius to construct the first aluminum beam analytical balance, which revolutionized balance design. A more modern advance in balance construction was the development of substitution weighing, in which one side of the beam is constantly loaded. The Swiss firm created by Erhard Mettler popularized balances of this type, with production dating back to 1947 (see sidebar). And beginning in 1948, the design of balances started to move in the direction of single-pan devices.

In subsequent years, manufacturers equipped balances with a rider mass that could be moved along the beam to augment small gravitational torque changes. Because air currents and humidity affected the operation of these balances, the working parts were enclosed in a glass case. And in 1955, Sartorius developed the first microbalance for weighing under standard ambient conditions.

The evolution of the chemical balance led to technical refinements such as pan brakes, magnetic damping of beam oscillation, built-in weight sets operated by dial knobs, and microscopic reading of the angle of beam inclination, which also led to the development of the microbalance.

Far from the simple tare systems of old, modern balances are capable of calibrating automatically for differences in ambient temperature, humidity, gravity, or atmospheric pressure. For example, instruments such as the Ohaus moisture analyzer allow accurate weighing while using fast heating to raise samples to up to 180 °C. In some cases, monitored parameters are coupled to regulatory guidelines, as in the Sartorius ultramicro and microbalances that warn users when the weight on the balance is below the minimum allowable sample weight required by the United States Pharmacopeia. Today, although the fundamentals of balance technology remain relatively the same, the applications have burgeoned, with design factors dedicated to improving user-friendliness, and increased sturdiness and portability of balances overall. Today, balances remain a flourishing laboratory instrument sector including manufacturers such as Mettler-Toledo, Ohaus, Sartorius, and Shimadzu.

X-ray Crystallography

In 1912, German physicist Max von Laue discovered that crystals not only diffract X-rays but also belong to a specific band of wavelengths in the electromagnetic spectrum, which linked crystallography with electromagnetic wave theory. More recently, Rosalyn Franklin's pioneering model-building method of structural determination enabled James Watson and Francis Crick, in 1953, to elucidate the structure of DNA. Since that time, scientists have used X-ray diffraction patterns to aid in the study of molecules.

In a typical X-ray diffractometer, in order to solve the structure, the unit cell and space group must be determined from the diffraction of the X-rays using the Bragg equation. Fortunately, since the late 1950s, with the advent of computers, scientists have been able to determine the precise 3-D atomic structure of large molecules such as enzymes and proteins more effectively. Today, having this ability, scientists are able to determine accurate molecular structures. And knowing the structure of biological molecules, as a prerequisite in drug design and structure-based functional studies, has greatly aided scientists in the development of effective therapeutic agents and drugs.

Crystallography has reliably provided answers to many structure-related questions, enabling scientists to eventually determine how the common cold and other viruses enter human cells. Since the introduction of X-ray crystallography more than 50 years ago, scientists from Dorothy Crowfoot Hodgkin on have solved the 3-D structures of biological molecules and entered 7500 protein structures into the Protein Data Bank. As more difficult proteins come under study, companies such as Rigaku/MSC and Veeco have developed imaging and high-throughput systems geared to optimizing crystallization for X-ray analysis. And X-ray system manufacturers such as Bruker AXS, Oxford Cryosystems, Rigaku/MSC, and Siemens are equipping researchers with the necessary instrumentation that is now commonly used in everyday scientific applications around the world.

All of these instruments, as well as a host of other so-called minor instruments, have revolutionized chemistry as much if not more than the big-ticket chromatography and spectroscopy systems combined, making them an integral component of the chemical enterprise, in sales and in the lab. ◆