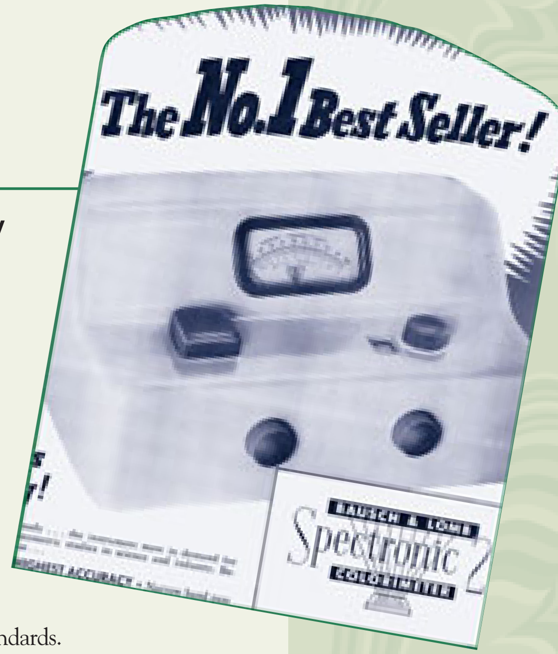
Seeing with Spectroscopy

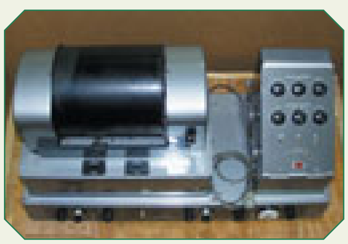
Instrumental "eyes" give chemistry a window on the world.

DAVID FILMORE



At the time of the U.S. entry into World War II, much was known about the electromagnetic spectrum. Analyzing the properties of visible light had been a pursuit of great thinkers at least since Aristotle recognized its connection to color in the 4th century B.C. In the 19th century, attention turned to the invisible as well, from Friedrich Wilhelm Herschel's discovery of the infrared (IR) region in 1800 to Paul Villard's observation of gamma radiation in 1900 (ultraviolet light and X-rays were uncovered in the interim). In 1923, Chandrasekhara Venkata Raman discovered the inelastic light-scattering effect that bears his name.

By the end of the 1930s, using light absorption and emission as a tool for chemical analysis was not a foreign subject to analytical chemists, and several instruments had been designed. For example, by 1906, Walter Noel Hartley commercialized the spectrograph in Britain with the Adam Hilger company. Adam Hilger also marketed an IR instrument that used a rock salt prism in 1922. Franz Schmidt & Haensch in Germany began producing a visible spectrometer in the same time period.



These instruments and others provided a new way to look at previously intractable chemical problems, but they still left a lot to be desired in performance. For example, although spectrographs of the type designed by Hartley—and marketed by Hilger as well as other companies such as the Central Scientific Co.—gained in popularity, obtaining spectrums from these instruments involved many manual steps and laborious visual comparisons of photographic plates. In the 1920s, however, the technology for photoelectric devices, which could electronically detect light signals, was progressing.

This heralded the development of the spectrophotometer, which used photocells to detect signal intensities. Arthur Hardy, a physicist at the Massachusetts Institute of Technology, produced one of the first spectrophotometers, using cesium photocells, in the early 1920s. By 1930, he struck a deal with General Electric to manufacture the instrument, which became an important color analysis tool for companies such as International Printing Ink and the National Bureau of Standards.

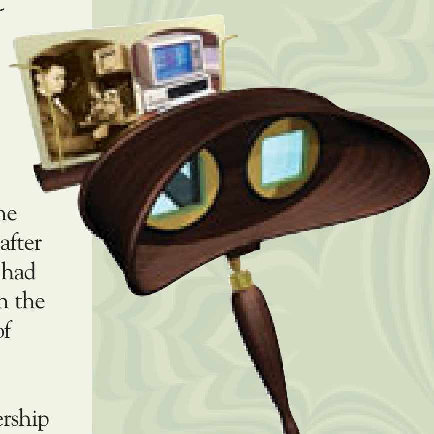
Instruments of War

As the possibility of American involvement in World War II grew, the ability to measure vitamin A and other vitamins in food was essential to ensuring the nourishment of soldiers. In 1941, Arnold O. Beckman (see sidebar) at National Technical Laboratories (NTL; renamed Beckman Instruments in 1950) saw an opportunity to design a spectrophotometer—ultimately the Model DU—that could fulfill this need. Its successful launch proved to be a pivotal point in the transition from a predominantly "wet" chemical analysis approach to a more automated instrument-based laboratory infrastructure.

The war, of course, brought on myriad needs beyond vitamin analysis. The United States was dealing with a major shortage of natural rubber during the war. The Office of Rubber Reserve, which was set up to develop synthetic rubber alternatives, contracted NTL, based on its reputation for manufacturing the DU, to produce a single-beam IR instrument to measure the concentration and purity of butadiene at every step of rubber synthesis. NTL shipped its first IR instrument, IR-1, in 1942 for a top-secret program for synthetic rubbers and for aviation fuels. The agreement with the government restricted sales of the IR-1 until after the war. But Perkin-Elmer—a company that had become the main source of precision optics in the United States—was also privy to the Office of Rubber Reserve meetings and recognized the potential of IR. Based on collaboration with American Cyanamid and the technical leadership of Van Zandt Williams, Perkin-Elmer began selling the Model 12 IR spectrophotometer in 1944.

Top: Spectronic 20, Bausch & Lomb ad, *Analytical Chemistry*

Center: Perkin-Elmer IR 21 spectrophotometer, *Made to Measure*, 1999



Markets Expand

After the war, the markets for UV-Vis and IR instruments widened as scientists began applying them more broadly to chemical analysis issues of the day. For example, the number of IR spectrometers in use in analytical laboratories went from a handful before the war to about 400 by the time it was over.

NTL was the major player in the UV-vis instrument market with the model DU and also the Model B, marketed in 1949, but other companies were entering the fray. Coleman Instruments had come out with a popular instrument in 1942, the Junior UV/Vis model, which was the first instrument with a direct-reading meter. And in 1946, Howard Cary, who was director of research and development at NTL, split from the company and formed Applied Physics Corp. The following year, Applied Physics offered the Cary 10 and 11 UV/Vis spectrophotometers, the first to have a double monochromator design, which afforded much less stray light from the UV-Vis source.

The commercial IR market remained predominantly a competition between Beckman Instruments and Perkin-Elmer in the years following the war, although Shimadzu introduced its first IR instrument, the LS-80, in 1950. In that year as well Perkin-Elmer launched its Model 21 spectrophotometer, which was the first commercially successful dual-beam instrument. Single-beam products, such as the IR-1 and the Model 12, required tedious manual replotting to obtain a standardized spectrum; by adding a reference beam, this step was avoided. The Model 21 soon became the best-selling IR instrument in the United States and had a big impact on expanding application of the technique to sectors ranging from pharmaceuticals to the perfume industry.

With the growing commercial success of UV-Vis and IR instruments, companies began to look at other forms of spectroscopy. Applied Physics expanded its product line in the early 1950s by commercializing one of the first Raman spectroscopy instruments, the Cary 81. But it had nowhere near the analytical power of today's Raman instruments. It was in 1964, when gas laser sources were introduced and the weak inelastic scattering signal could be better exploited, that the Raman instrumentation industry began in earnest, with an updated Cary 81 and the newly developed Perkin-Elmer LR-1 and Spex Industries 1403 Ramalog.

During World War II, researchers at the National Institutes of Health (NIH) worked on identifying antimalaria drugs by using fluorescence. This research led to the use of fluorescence as a general tool for scientific research. Robert Bowman and his team at NIH subsequently developed the first spectrofluorometer, which was commercialized in 1956 by the American Instrument Co. as the AMINCO-Bowman spectrofluorometer.

Other techniques became available. X-ray fluorescence spectroscopy, an important elemental analysis tool, began to hit the market around this time. And atomic absorption spectroscopy began on a path of commercial success in 1963 with Perkin-Elmer's Model 303 AA.

The phenomenon of nuclear magnetic resonance (NMR)—nuclear spin transitions that occur in the presence of microwave frequencies in a magnetic field—was first observed in 1946 by Felix Bloch at Stanford University and Edward Mills Purcell at Harvard University. Russell Varian licensed Bloch's patent on the technology and, in 1948, formed Varian Associates with his brother Sigurd to commercialize the technology for chemistry applications.

Varian's first instrument was the HR-30, shipped in 1952 to several large companies, including Humble Oil, DuPont, and Shell. In 1955, the HR-40 was offered, which added the now obligatory feature of sample spinning, as well as magnetic field stabilization. The company finally achieved its first financial success in NMR in 1958 with the higher-field-strength HR-60. The field became competitive with the entry of the first commercial NMR from the German company Bruker in 1963.

Toward the Black Box

Chemists' increased reliance on spectroscopic instrumentation created more needs for the instrument developers to address. For example, providing further automation so the techniques could be done faster was a big priority. In 1954, Beckman released its DK-1 and DK-2 spectrophotometers, which covered the spectrum from the UV to the near-IR. These were the first successful instruments that automatically recorded spectra from the spectrometer to plotting paper, eliminating a time-intensive manual step.

A trend began in the mid-1950s to develop instruments expressly for the routine use of the individual bench chemist, that is, low-cost instruments with black box simplicity and rapid results. UV-Vis spectrometers were the closest to fitting

Above: Arnold O. Beckman with his DU spectrophotometer, courtesy of the Chemical Heritage Foundation.

ARNOLD O. BECKMAN

Arnold O. Beckman was both an entrepreneur and a research chemist interested in measuring chemical properties. Beckman was born in 1900 in Cullom, IL. In 1934, Beckman was presented with a problem of measuring acidity for a citrus-processing plant. He designed and developed an acidimeter—the forerunner of the pH meter. He applied for a patent and launched National Technical Laboratories in 1935. Beckman went on to change the course of analytical instrumentation with the DU spectrophotometer and subsequent instruments.

Beckman, Howard Cary, and others at NTL set out to build the right optics to go with the electronics used to amplify the signal in the popular pH meter. After receiving a wartime priority designation by the government—so it could obtain highly-in-demand quartz crystals to make prisms—and designing several prototypes, the team produced, in 1941, the Model DU spectrophotometer. Its spectral range stretched from the UV through the visible spectrum, and it housed both the electronics and the optics within the monochromator for a simple and affordable design.

NTL sold—at $723 each—18 DUs in 1941 and 1954 DUs in 1942, a substantial market at the time. In 1952, Beckman Instruments went public, securing funds for global expansion and acquisitions. In 1998, Beckman Instruments acquired Coulter Corporation, and together, they operate as Beckman Coulter. In 1999, Arnold O. Beckman was presented the Public Welfare Medal, the National Academy of Sciences' highest honor. This pioneer of instruments died in his sleep on May 18, 2004.

this description already, but in 1954, Bausch & Lomb introduced the Spectronic 20, the first low-cost spectrophotometer with a diffraction grating used for light dispersion. It quickly became a highly popular instrument for quick bench-top assessments of solutions and is still commonly used in teaching laboratories.

IR instruments such as the Model 21 and Beckman's IR-3 were still too expensive for nonspecialists in spectroscopic analysis to make the investment. Perkin-Elmer decided to target a new market by designing an instrument with specific features that simplified the manufacturing process. This resulted in the introduction of the Model 137, a low-cost IR instrument.

The simplification trend made its way to NMR in 1961, when Varian sold 120 of its new A-60 instruments. The A-60, which came with a catalog of NMR spectra for 700 different compounds, was, of course, not a benchtop device, but it was a smaller, more affordable, proton-only instrument that helped establish NMR as a standard tool for organic chemists.

The FT Factor

In 1956, Alastair Gebbie in London designed the first instrument that replaced a light-dispersing grating with a Michelson interferometer and used Fourier transform (FT) algorithms to obtain an IR spectrum (see chapter, "Computers and Automation"). This allowed the recording of the spectral range simultaneously to substantially improve the quality of spectra and simplify the process. But the computing power that was required for efficient FT processing wasn't available in the 1950s. The development of the Cooley and Tukey fast FT algorithms in 1964 decreased this burden somewhat, and, at the same time, computers were improving.

Digilab introduced the first commercially available FT-IR, the FTS-14, in 1969. It covered the entire IR region with a fast-scanning interferometer, and the FT operations were completely computer-controlled. This marked the beginning of the phaseout of dispersive IR instruments. It also provided an opportunity for new companies to enter the IR market. Both Bruker and Nicolet (now part of Thermo Electron) came out with FT-IR spectrometers in the mid-1970s, and Bomem introduced its first FT instrument in 1980. Perkin-Elmer, which didn't launch an FT-IR instrument until 1981, found itself in an increasingly competitive market. In 1988, the Japanese company Horiba collaborated with the U.S. company Maidak to transfer technology on FT-IR spectrometers.

Varian, which had expanded its market reach by acquiring Applied Physics in 1966, integrated FT into NMR with the Model XL100. Raman spectroscopy finally joined the FT bandwagon in 1988 when Bruker commercialized a Raman microscope accessory to its FRA 106 FT-IR.

The rise of the personal computer in the 1970s further added to the ease and efficiency of performing spectroscopic experiments. Perkin-Elmer marketed its 460 AA spectrophotometer together with a computer for external control. Hitachi launched its 340 microprocessor-controlled UV-Vis/near-IR spectrophotometer in 1977, followed by a string of similar instruments from Beckman, Perkin-Elmer, and Shimadzu. By the mid-1980s, knobs and controls were largely disappearing from the instruments in favor of the computer keyboard and then the mouse.

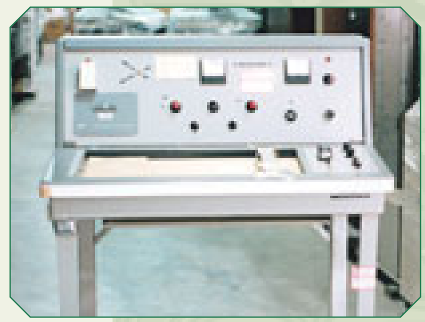
Hewlett-Packard entered the spectrophotometer market in 1979 with the first application of another silicon-related innovation, the diode array detector. The HP8450 spectrometer could scan the visible region in a single second.

The Modern Market

Hundreds of companies now produce spectroscopy instruments in all of their "colors," with the result that spectroscopic methods are continuing to undergo substantial transformations. For instance, the development of increasingly higher-field instruments and the introduction of hyphenated techniques, among other advances, are continually escalating the importance of NMR for protein studies from companies such as Bruker BioSciences, JEOL, and Varian.

Over the past decade, IR and Raman have been spreading out of the lab to applications ranging from process manufacture monitoring to direct environmental field analysis because of the development of visible and IR photodiode array detectors that allow commercialization of simplied handheld analyzers. Fluorescence spectrophotometry is another fundamental analytical technology undergoing a transformation. Life science researchers who applied fluorescence vigorously to endeavors such as the Human Genome Project are switching from conventional spectrofluorometers to fluorescence-based microplate readers designed more expressly for their purposes—proving that whatever the need, spectroscopy will continue to adapt, remaining the essential eyes of science. Companies such as Renishaw, Jasco, JY Horiba, PerkinElmer, Varian, Thermo, and Shimadzu continue to advance the state of these spectroscopic arts.

And finally, it must be noted that the trace metal spectroscopies, in all their manifestations, have become a fundamental tool of the modern laboratory. From the early days in flame photometry, companies such as JY Horiba, PerkinElmer, Agilent, Shimadzu, and Thermo have provided a dizzying array of graphite furnace atomic absorption, inductively coupled plasma, and inductively coupled plasma mass spectrometry instruments for environmental, semiconductor, and clinical chemistry determinations. ◆



Above: Console of the Varian-60 NMR, *Made to Measure*, 1999