Scientific Instruments

Caspary Gallery of
The Rockefeller University

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THE NEWS of science usually deals with what a scientist has found out and what the benefits may be. How a scientist finds out—the methods and instruments he uses and develops in the course of his research—very rarely gets detailed coverage. Yet the progress of science has depended on the invention and refinement of tools and techniques for testing theories and "seeing" more deeply into the nature of things.

As a research institution in the forefront of progress in the medical and biological sciences for 85 years, The Rockefeller University, founded in 1901 as The Rockefeller Institute for Medical Research, has made many contributions to the development of new instruments and techniques. Its scientists have played a particularly significant role in the application of physical and chemical methods to the life sciences. Many research techniques and devices that originated at the University are still in use in laboratories throughout the world. This is a record of achievement shared by the scientists and the skilled craftsmen—the instrument makers, glassblowers, and others—who have helped the scientists extend the perceptions of their senses, refine the precision of their techniques, and win freedom from routine for creative research.

Obsolescence is inevitable as technology advances. As new methods were introduced, many items were summarily discarded and lost to the archivist and historian. It is not by chance that so much of what has survived is optical and physical in nature, for many of the tools designed by these branches of science are still useful. The exhibit described here consists of some of the survivors, assembled and inventoried by Anthony Campo, former chief pharmacist and superintendent of purchases, and his successor James Stewart. Some of the items are instruments developed here and constructed in the University shops; others illustrate modifications of existing tools or techniques by University scientists; others are of interest because of their association with the work of individual scientists or laboratories. A few are still being used. All are significant pieces in the mosaic that is the history of this institution.

Exhibits

The items are numbered in sequence beginning with the alcove to the left, as you face the main wall, and continue along the wall to the alcove at the right.

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1 Florsdorf-Mudd freeze-drying apparatus introduced in the 1930s. This model was the prototype for the more sophisticated commercial freeze-dryers of today. It was designed for preserving biological specimens that break down when held in solution. In the freeze-dryer, the specimen is dried from the frozen state under high vacuum, which sucks away moisture by the process of sublimation and deposits it in a cold trap at −80°C (dry ice and alcohol).

2 Glass enclosures used in 1932 by Dr. Louis O. Kunkel for studies of the transmission of plant infections by leaf hoppers. Plant diseases, like animal diseases, can be transmitted by insect carriers (vectors) of infecting agents such as viruses and mycoplasma. The glass enclosure, covered at the top by fine netting, was placed over the "test" plant. Then leaf hoppers that had fed on diseased plants were injected through the netting. Kunkel and his associates made important contributions to the knowledge of mosaic virus diseases of tobacco, sugar cane, and Indian corn, and of a disease of asters known as "yellows."

3 Bacterial densitometer designed about 1925 and used by Dr. Frederick L. Gates (see 6). The densitometer, designed to measure the turbidity of growing bacteria, indicated the rate of bacterial multiplication. The platinum loop was "buried" until it just became invisible, and the scale was read before the loop was withdrawn and heat-sterilized. This model was soon superseded by electrical spectrometers.

4 Culture flask designed by Dr. Hideyo Noguchi and made by Corning Glass Company, with his name etched on it. Used in the 1920s for growing anaerobic spirochetes of the *Leptospira* group, microorganisms responsible for a number of infectious diseases in man and other mammals.

5 Culture flasks used by Dr. Thomas M. Rivers for producing smallpox vaccine by growing vaccinia (cowpox) viruses in cultures of living chick tissue. Between 1927 and 1933, Rivers and his associates developed a simplified method of growing the vaccinia virus on a relatively large scale. Their work involved the first cultivation of a virus in tissue culture for use in human beings. This method has since been used extensively for the cultivation of many other types of viruses.

6 Culture flasks designed and made by Dr. Frederick L. Gates, son of Frederick T. Gates, who played a key role in the founding of The Rockefeller Institute for Medical Research. Collodion sacs were suspended in the flasks, which contained proteinaceous culture medium. The dialyzable medium constituents allowed some types of microorganisms to be grown within the flasks, free of proteins, permitting the withdrawal and study of protein-free microorganisms.

7 Culture flasks designed for growing microorganisms on a large surface.

8 A bottle containing some of the first tobacco mosaic virus isolated, in crystalline form, by Dr. Wendell Stanley in 1935. This work provided a great impetus for chemical studies of viruses. Stanley shared the Nobel Prize in Chemistry in 1946.

9A Bausch & Lomb microscope from the early 1900s with double nose piece and a substage disc with a choice of four openings ("diaphragm stops") to vary the amount of light on the specimen to be examined.

9B Zeiss monocular microscope purchased before 1919, with triple nose piece, rotating stage and complex substage condenser (a system of lenses for concentrating light on the specimen). Used by Drs. Harold L. Amoss, Edmund V. Cowdry, and Stuart Mudd.

9C Zeiss Bitukni microscope purchased for the Pathology Division in 1925, the first combination monocular-binocular microscope manufactured.

9D Leitz binocular microscope, 1931, with mechanical and revolving stage, and with complex substage condenser. Used by Dr. Thomas M. Rivers, leader in virus research and director of the Rockefeller Hospital, 1937–1955.

10 Scalpels (bistouries) with hollow handles, made in France and chosen for use by Dr. Alexis Carrel, whose pioneer work in blood-vessel surgery won him a Nobel Prize in 1912—the first for medicine to be awarded to a scientist in America.

11 Dr. Florence Sabin's personal microscope, donated to the University upon her retirement in 1938. This was a top Spencer binocular microscope of the time.

12 Very early Schultz-Dale Chambers, about 1920, brought to the University in 1923 by Dr. Karl Landsteiner. The study of anaphylactic reactions of smooth muscle in vitro was begun by Schultz in the United States and by Henry Dale in Britain. The test chamber was fixed within a constant-temperature bath, and arranged for replacement of the bath by a siphon system. Within the chamber, a strip of smooth muscle from a sensitized guinea pig—gut or uterine horn—was fixed at one end by a platinum hook fused in a glass tube through which oxygen bubbled. The free end of the tissue was attached to a thread rising to exert pull on a writing lever bearing on a kymograph drum (items 36A,B,C). When antigen was added to the bath, the sensitized muscle contracted and registered its contraction on the smoked drum. The chambers shown here were very early models, offering minimal bath volumes.

13 Set of Warburg flasks used in enzyme research. The flasks are fitted to individual manometers and are shaken at constant temperature. The rate of oxygen utilization during the reaction between enzyme and substrate can be measured, and CO_2, also produced, can be absorbed and measured separately.

14 Centrifuge tubes made to the University's specifications, originally designed to grow 50 milliliter volumes of streptococci and pneumococci for chemical studies. The University owned the molds.

14A Precision cataphoresis cell developed by Dr. Theodore Shedlovsky. To watch migration within an electric field, a flattened cell is used for microscopic observation. The model

shown contains such a flattened cell sealed to a unit which permits use in either the horizontal or vertical position. The cell is filled and washed via the two-way stopcock. It was much used in war work.

14B Student microscope around 1900, with four "diaphragm" holes in the substage plate.

15 McLeod Gauge developed and built for Dr. Walther F. Goebel in 1940 by the University's Glassblowing Shop. Measures—in inches of mercury—the degree of vacuum (negative pressure) in a contained space. Used for micro-distillation in vacuo of sugar compounds.

16 Melting point apparatus designed by Dr. Lyman C. Craig and Mr. Otto Post. An aluminum slab with embedded thermometer is slowly heated electrically. The crystals, held between two cover glasses and watched by polarized light, are observed through the microscope. At the moment of melting, the liquid crystals darken. The apparatus shown here incorporates a Spencer monocular microscope purchased in 1919.

17A Swedish angle centrifuge, circa 1930–1935, donated to Dr. Karl Landsteiner by the manufacturer in 1938. Optimal angle was patented in Sweden because of its efficiency in centrifuging biological materials. By spinning samples at high speed, these machines use centrifugal force to separate particles of differing weight. The special Swedish tubes for use in the square trunnion cups are shown, noncircular in cross section. These narrow tubes were much used when collodion agglutination was in vogue.

17B Angle centrifuge, adapted from the Swedish principle, developed by Mr. Josef Blum in the University's Instrument Shop in the 1930s. Blum, head of the Shop from 1939–1954, produced a centrifuge that operated at speeds up to 20,000 rpm. Blum fabricated his rotors of a solid block of light metal drilled radially to accept sample tubes inclined in fixed positions between horizontal and vertical. The drives were electric motors, and Blum designed a self-centering direct drive that would permit slightly unbalanced rotors to find their natural center of rotation. This model was the prototype of centrifuges now in use in biological laboratories everywhere.

18A Coleman Jr. spectrophotometer used in the laboratory of Dr. Lyman C. Craig. In 1964 the manufacturer determined that this 1940 model, series six, #003, was the earliest model still in use and presented Dr. Craig with (18B) a gold-plated spectrophotometer, Model 6C, serial 58288. Spectrophotometry is a method of chemical analysis based on the absorption of light of a specified wave length or frequency. A simple spectrophotometer consists of a source of radiation such as a light bulb, a prism or grating for dispersing the light so that only a limited wave length irradiates the sample, and a detector such as a photo cell for measuring the amount of light transmitted by the sample. The weight of the later model was only a fraction of the first's.

19A Quartz conductivity cell for precise determinations of electrical conductance in solutions, designed by Dr. Theodore Shedlovsky. Quartz was chosen for its insolubility rather than glass, which is too soluble in water to allow fine readings. Truncated platinum cones for electrodes are sealed to a special Jena glass as a sidearm. Since quartz and glass do not fuse, Otto Hopf, the glassblower, ground both separately and mixed them in different ratios to effect a "graded seal," visible on the sidearm. (With

the best quality water, electrical conductance could be determined on solutions as dilute as 0.00001 molar.)

19B Pyrex conductivity cell, also designed by Dr. Shedlovsky, for studying the conductance of more concentrated solutions. Pyrex is adequate, but again graded seals with Jena glass are necessary.

20A–C The glass electrode as a precision research instrument was developed at the Rockefeller Institute by Dr. Duncan A. MacInnes and his colleagues. The instruments in the collection submitted by Dr. Theodore Shedlovsky are a grateful token of this collaboration.

A. Compton quadrant electrometer, 1926. Electrometers are used to measure electrical charge by mechanical forces exerted on a charged electrode in an electric field. Soft glasses serving as glass electrodes were introduced in the 1920s and were adopted to the measurement of pH, the acid-base balance in living tissues. The quadrant electrometer, insulated by amber and by solid sulfur at some points, was the first instrument capable of responding to the passage of ions through the glass. The metal outer case with its window lens (1 meter focal length) is removed to display, near the base, tiny hollow quadrants close by a vane which resembles the shape of a dog biscuit. Opposite pairs of the quadrants are connected; one quadrant can be removed to create asymmetry between the two pairs. Between the quadrants passes a suspended quartz fiber, metallized, bearing a tiny mirror. Changes in potential alter the path of light reflected through the lens and focus on a scale, at a distance of 1 meter.

B. Early glass electrodes of Corning 0–15 glass. The first glass electrodes were fabricated by Drs. Duncan A. MacInnes and Malcolm Dole. The University's glassblower, Otto Hopf, then made glass electrodes like those shown. Basically, the glass electrode is a thin-walled glass membrane that permits passage of hydrogen and hydroxyl ions and determination of the resultant pH. The glass electrode became practicable as a laboratory tool when vacuum tubes were developed to amplify the current of the string galvanometer.

C. Working glass electrode assembly in stand. Dr. MacInnes and his group developed a basic stand of nonconducting Lucite holding the component parts shown but actually encased in shielded metal and incorporating a fan and dials to read pH directly for the first time. The trick was MacInnes's stopcock allowing cyclic flushing of the tube and filling with test solution, and connection to a reference mercuric chloride half-cell through a liquid junction. This system was adopted widely throughout Rockefeller. All were fabricated by a technician in Dr. MacInnes's laboratory. Glass electrodes are now universally used in determining pH directly, and ions other than H^+ and OH^-.

21 Beckman pH meter purchased for Dr. Oswald T. Avery in 1938, repaired and updated in 1958. This is an early commercial model using the MacInnes principles. All modern laboratories have some kind of pH meter; most depend on electrochemical principles.

22 Precision quartz pyknometer designed by Dr. Theodore Shedlovsky for determining the specific gravity of a solution by weighing a known volume. The usual apparatus resembles a flask with a glass stopper. In this novel version made of quartz in U-shape,

precision quartz capillary tubes are fused to its ends. Calibration of the contained column has been made for various temperatures, as seen through the magnifying glass.

23 Tensiometer invented by Dr. Pierre LeComte du Noüy in 1922 for making rapid and accurate measurements of the surface tension of liquids, particularly of undiluted blood serums. DuNoüy's model was put into commercial production by Central Scientific Company of Chicago (as displayed). A steel wire serves as a torsion element which supplies upward force, through a lever arm, to a platinum-iridium ring resting on the liquid. The force required to separate the ring from the liquid surface is read directly in dynes on the circular scale.

24A Simple Voland balance with free-swinging pans. The object to be weighed is placed on the left-hand pan. Weights from the box are laid on the right-hand pan. Fine balancing is completed by moving the small platinum rider on the upper right beam. The rider indicates the third and fourth decimal figures of the weight. Used in the laboratory of Dr. Karl Landsteiner in the early 1930s.

24B Sartorius analytical balance of the type designed by Dr. Pierre Curie in France about 1925. "Air cups" are used to damp or diminish the successive swings of the pointer across the scale. Weights are placed mechanically on the right-hand beam. Used by Drs. Duncan MacInnes, Theodore Shedlovsky, and Lewis Longsworth.

24C Seederer-Kohlbusch "chainomatic" balance. The weight of the links in a gold chain replaces the mechanical addition of separate fine weights. Damping is done magnetically by suspending a plate between the poles of a magnet (upper right). Used by Dr. Lyman C. Craig.

24D Bunge Micro Balance, one of the first mechanical balances to weigh to the sixth decimal place (to 1 microgram). The scale is read at the top of the balance by reflected light. Static electricity is a great problem in weighing very tiny amounts of a substance. Charged powders will not drop from the spatula into the pan and can fly into the air. The balance displayed here carries radioactive Plutonium 210, which emits alpha particles, ionizes the air, and thus discharges static electricity. Used by Dr. Donald Van Slyke in the 1920s.

24E "Multiplying" balance of the type originally introduced to weigh snuff and other light materials. The beam pivots at a 10:1 ratio, so the weights added to the forward pan must be 10 times as heavy as the material to be weighed. Small precipitates (about 30 to 200 milligrams) could be weighed rapidly. This balance was brought from Europe to the University by Dr. Karl Landsteiner and used extensively by Dr. James van der Scheer.

25A Sterile filtration equipment used prior to the development of membrane filters: French Chamberland "bougies," assortment of porosities from L11 to L3. These were thrust through rubber stoppers and suspended in suction flasks.

25B Berkefeld filters with mantles and "suction tubes" to maintain fluid over the candle as the liquid dropped. Four sizes are shown.

25C Berkefeld filter for sterilizing rabbit serum, assembled exactly as it was used in Dr. Karl Landsteiner's laboratory in 1932.

25D Seitz filter for positive pressure, utilizing an asbestos pad.

26 Lauritsen electroscope, circa 1940, used by Dr. Fritz Lipmann. When charged with static electricity, the arms (vanes) opened. The speed with which the arms closed when radioactive phosphorus was brought near related to the amount of radioactivity in the sample. At present beta radiation and gamma radiation are measured routinely by sophisticated instrumentation and print-outs.

27 Pulfrich refractometer purchased circa 1920 and used by Drs. P. A. T. Levene, Walter A. Jacobs, and Lyman C. Craig. Used to measure the refractive index of various substances; that is, the deflection from a straight path undergone by a beam of light on passing obliquely from one medium (such as air) to another (such as water) in which its velocity is different.

28 Zeiss dipping or immersion refractometer of the 1915–1920 period. Protein dissolved in a solution changes the refractive index of the solution. The concentration of protein can be measured in a sample by dipping the crystal tip of this instrument into the sample cup, illuminated from the bottom. Temperature control must be exact.

29 (Hanging overhead.) Laboratory glassware made in the University's Glassblowing Shop to the specifications of the scientists.

30 Rotating disc viscometer of MacMichael type, used in Dr. Alexis Carrel's laboratory in the 1920s by Dr. Pierre LeComte du Noüy. Provided a gauge of the viscosity of a liquid by measuring its resistance to rotation of an immersed metal plate bearing two "wings." The disc is suspended by a torsion wire bearing a tiny mirror to record the twist in the wire caused by the viscosity.

31 Saccharimeter of 1915–1920 period with box of tubes. Used for the chemical analysis of sugar solutions, a specialized area of polarimetry.

32 Original half-shadow ellipsometer developed by Dr. Alexandre Rothen in the early 1940s to measure the thickness of films only one or a few molecules thick. It was constructed by Josef Blum in the University's Instrument Shop. Light polarized in a plane becomes elliptically polarized after reflection from a metallic surface. At the end of the last century, the German physicist P. Drude showed that a monomolecular film covering the metallic surface would shift the orientation of the ellipse. This shift could be used to calculate the thickness of the monomolecular film. The term "ellipsometer" was coined in 1944 by Dr. Rothen to describe his optical instrument for determining the ellipticity of reflected light; with it, thickness of molecular films could be measured with an accuracy of ± 0.2 Angstrom units, or about one billionth of an inch. This first ellipsometer was a visual instrument. The apparatus was provided with an original half-shadow device equivalent in function to the half-shadow of the Lippich polarimeter. The half-shadow ellipsometer became obsolete when photomultiplier tubes were introduced.

Photograph shows a recording ellipsometer. This improved instrument with photomultiplier tube provides a signal that is amplified and recorded on a strip chart and a tape recorder. It can measure an absorbed layer *during* its formation. This particular instrument incorporates (left side of the photograph) one of the three extant polarim-

eters of this type built in Germany (the others are located at the National Bureau of Standards and the University of Illinois). This polarimeter was purchased in 1920 at a cost of $10,000, an unheard-of amount for the purchase of a scientific instrument in those days.

33 Nickerson "decade" photometer, used by Dr. Donald D. Van Slyke. This photometer was a practical means of ascertaining the plasma volume of patients. A serum sample was drawn in advance as a "blank." Then Evans Blue dye was injected intravenously and serum, now blued, was drawn again. The serum color was matched by switching calibrated blue plastic discs, carried in two "decades" within the drum, into the visual field over the "blank." The dye value was read directly from the slot on top of the drum.

34 Pocket refractometer, circa 1900. A prism divides white light into the visible spectral colors. The material to be examined is placed between the legs, and absorption of colored bands is noted as identification. There are three principal adjustments, including positioning of mirror and of slit.

35 Early model Schmidt & Haensch polarimeter used by Drs. P. A. T. Levene and Walter A. Jacobs. The polarimeter measures the optical activity of substances in solution. Optically active materials possess the power of rotating the plane of polarized light, a rotation measured in a beam of polarized light passing through the sample of a pure material and observed through a Nicoll prism in the eyepiece of the instrument. Since there is a great difference in the biological activities of the different optical isomers of organic compounds, polarimetry is widely used in biochemical research to identify the molecular configurations.

36A Kymograph, 1915 model, with spring-wound motor and replaceable vanes for control of speed. There are two markers or styli for "writing" on smoked paper. A kymograph is used to record muscle activity and other physiological events such as heartbeat and breathing. Glazed paper is attached to the drum and smoked by revolving it over a benzene flame. The drum is then placed on a shaft of a spring-wound motor or, in later models, an electric motor, and set to turning. The activity being studied is recorded by a stylus scratching a curving line on the sooty paper. Improved kymographs used an ink-writing mechanism rather than a smoked drum. In the device for smoking glazed paper, illuminating gas, saturated with benzene or toluol, ascends the wicks and burns with a smoky flame along the perforated finger. As the drum holding the paper is rotated by hand, a layer of carbon particles is deposited on the glazed paper.

36B Brass kymograph, dating back to the 1920s. Used by Dr. Samuel Meltzer, the University's first physiologist, and his associate, Dr. John Auer; later used by Dr. Alfred E. Cohn, a major contributor to cardiological research; and then turned over to Dr. D. Wayne Woolley, known for his work in bacteriology, physiology, and biochemistry.

36C Jaquet time marker for inscribing uniform time intervals in the turning kymograph drum, used with 1.5-volt dry-cell battery and a variety of styli for use on smoked paper or for ink writing. The marked intervals allow calculation of the time required for each portion of a physiological event, such as a complete muscle contraction, to occur. The record of the event itself is recorded on the kymograph drum by a stylus attached to another lever.

37A Portable cardiac pacemaker unit developed by Drs. Lawrence Eisenberg and Alexander Mauro at The Rockefeller University, 1961–1964, in collaboration with Dr. W. W. L. Glenn of the Yale University School of Medicine. The patient moved freely, carrying a battery operated transmitter unit in his pocket. Electrical impulses were transmitted to a tuned coil under the skin and thence to the heart. 37B is a later version of this unit; the lower half of the casing is the replaceable battery. Portable units became possible with the introduction of transistors. The first cardiac pacemakers utilized external electrical stimulators, connected to the heart by wires through the skin. To overcome the danger of infection introduced by wires through the skin and yet retain control over the stimulating parameters, an external unit that transmitted electrical impulses to a tuned coil under the skin and thence to the heart was developed at Yale University School of Medicine by Mauro and Glenn. It was then introduced on a patient, January 29, 1959, at Grace-New Haven Hospital, the first total implant so used. 37C. The original line-powered vacuum tube transmitter is shown. An external antenna, placed on the chest over the site of the implanted coil, was connected to the transmitter by a 30-foot wire to allow the patient to move around his hospital room.

38 Kjeldahl digestion and distillation apparatus of the "semi-micro" size as used by Dr. Donald D. Van Slyke for the determination of nitrogen. One digestion flask of the original Kjeldahl apparatus, preceding the semi-micro version, is shown. Protein was digested by sulfuric acid and catalyst over gas flames, with vapor vented. Nitrogen, trapped in the form of ammonium sulfate, was subsequently released as free ammonia and titrated.

39A Original metal model of countercurrent distribution apparatus developed by Dr. Lyman C. Craig in 1940 for the separation of complex chemical mixtures. (39B and 39C are larger versions of the original.) A compound is placed in an apparatus that repeatedly brings together and then carries away separately two immiscible solvent fluids. In the process, each solvent carries along those substances in the compound that are more highly soluble in that particular fluid. The principle is illustrated in the four glass separating funnels (39D). The upper phase of tube one is shifted to tube two and fresh upper phase is placed in tube one. Four such transfers are shown. The lower colored compound is partitioned to the right. The first models had cylinders drilled into steel, arranged for "tumbling" the fluids and then a pause for phase separation before the upper phases were moved along one space. Later models, produced commercially, are made of glass, and some of these automatically operated units are capable of up to 1,000 transfers in a single run. 39E is a small glass, hand-operated prototype of these giants, which consist of 1,000 receptacles mounted along a motor-driven rocking axle. A small quantity of the drug or other preparation to be tested is placed in a receptacle containing the solvents. The contents are agitated mechanically and then allowed to separate, after which the lighter solvent is decanted into the next receptacle. The countercurrent distribution technique made possible the isolation of many rare drugs, hormones, and vitamins in pure form for the first time. During World War II the introduction of complex drugs for preventing and treating malaria created a need for ways to determine exactly their chemical purity. The large molecular weight and instability of these compounds made this a difficult task. Craig brought to this problem his countercurrent distribution technique.

40 Glass apparatus made personally by Dr. Edward L. Tatum to study the growth response of bread-mold, *Neurospora crassa*, on nutrient agar with which the long growth tube is partially filled. This equipment permits a regulated air stream to be humidified, filtered, and modified in the large bubbler that is inserted between the short and the long growth tubes. The sidearms permit introduction of substances or culture inocula at various positions on the surface of the nutrient agar. Both the small bubbler at the end of the growth tube and the large bubbler are liquid-filled traps to remove or add volatile substances that are in the air stream. Through studies of the metabolism and genetics of microorganisms, Tatum, a Nobel Prize winner in 1958, helped to prove that individual genes are encoded messages that regulate the synthesis of single proteins.

Item 41 has been withdrawn.

42 Cover from Time Magazine of June 13, 1938, photocopied.

42A Carrel-Lindbergh perfusion pump for the cultivation of organs, first used successfully in the spring of 1935 to cultivate the thyroid gland of a cat. This was the first time a whole organ had been cultivated in vitro. This version of the perfusion pump was developed and designed by Dr. Alexis Carrel and Colonel Charles A. Lindbergh, the famous aviator, who was invited to work as a volunteer in the Carrel laboratory. To maintain organs in vitro, they must be supplied with oxygen, salts, and nutrient by perfusing the blood vessels with the aid of a pump that moves the fluid through the blood vessels in pulses like heart beats. Full sterility had to be maintained, as there were no antibiotics at that time. The Carrel-Lindbergh pump was driven by a stream of compressed air made to pulsate by a rotating metal stopcock serving as a valve. The pulses were transmitted indirectly to the "control gas," a mixture of oxygen, carbon dioxide, and nitrogen, which served both to circulate and to oxygenate the nutrient fluid. The explanted organ was in contact only with glass and the fluid, which could be removed and renewed aseptically, and was automatically filtered while circulating. Glassblower Otto Hopf constructed the chambers, tubes, platinum screens, and glass valves of the intricate assembly.

Item 42B has been withdrawn.

43 Van Slyke apparatus for the exact measurement of oxygen and carbon dioxide in solution in blood and other fluids. Gas volumes were read at constant mercury pressure, controlled by the position of the side bulb. Developed by Dr. Donald D. Van Slyke between 1914 and 1920, this apparatus was so simple and convenient that it quickly took its place in the equipment of medical scientists. The model shown is a commercial version made about 1925. All of the "originals" have long since been discarded. Van Slyke's extensive contributions to clinical laboratory methods laid the foundation for many chemical and therapeutic procedures still in general use in hospital laboratories.

44A Automatic fraction collector designed by Drs. Stanford Moore and William H. Stein and built in the University's Instrument Shop in 1946. This instrument, used for 30 years, was invented to expedite chromatographic separations by collecting effluent fractions of given volume. The drops from the bottom of the column are counted by a photoelectric "eye," and the volume of each fraction is controlled by setting the dial on

the counter for a given number of drops. When the predetermined number is delivered to one tube, the circuit is closed, a motor rotates the rack one notch to position the next tube under the column, and the counter resets itself to zero. Overnight or over-the-weekend operation of the column is practical. Fraction collectors of this type have become standard items of commercially available laboratory equipment. In the laboratory of Moore and Stein this equipment was used in the development of methods for the chromatographic separation of amino acids, peptides, and proteins which facilitated the determination of the chemical structure of the first enzyme for which the chemical structure could be written—pancreatic ribonuclease. This research led to the award of the Nobel Prize in Chemistry in 1972 to Moore and Stein and to Christian B. Anfinsen of the National Institutes of Health.

44B Photograph of the first automatic amino acid analyzer developed by Moore and Stein in the 1950s, in collaboration with Dr. Darrel H. Spackman. Buffer of given pH is pumped through a column of ion exchange resin; the amino acids that are eluted serially from the bottom of the column are measured by monitoring the flowing stream with a colorimetric reaction; the intensity of the color is measured by a recording spectrophotometer. An analysis is complete in a few hours. The designers applied this equipment to the determination of amino acids in hydrolysates of purified proteins under structural study and to the free amino acids in mammalian tissues and physiological fluids. Thousands of such instruments are in use in biochemical laboratories around the world.

44C Photograph of a commercial model of Spackman, Stein, and Moore's automatic amino acid analyzer.

45 Photograph of model peptide synthesizer developed in 1966 by Dr. Bruce Merrifield, working with Dr. John Morrow Stewart and Nils Arthur Jernberg, the University's instrument design engineer. Merrifield developed the solid phase peptide synthesis technique for preparing peptides and proteins with predetermined sequence. The technique involves the use of an insoluble solid, polystyrene, as an anchor for the chain during synthesis. Merrifield and Dr. Bernd Gutte announced the first laboratory synthesis of a naturally occurring enzyme, the protein known as ribonuclease. (This coincided with a similar achievement by two chemists at the Merck Sharp and Dohme Research Laboratories, using a different technique.) The original apparatus shown includes a small glass reaction vessel (lower right) with its attendant "plumbing" and a programming unit (left). The rectangular pins in the rotating drum operate switches that control the pump, valves, timers, and shaker that fill and empty the vessel and mix the reagents. Amino acids are supplied from the six glass vessels (middle right). Solvents and other reagents are supplied from the large containers (above and right). To synthesize the complex ribonuclease molecule, it was necessary to connect its 124 amino acids in precisely the proper order to allow the long chain to fold spontaneously. The first amino acid group was bound to a small polystyrene bead, and the other 123 added one at a time. The peptide synthesizer automated the process and in the three weeks of continuous operation completed the 369 chemical reactions and the 11,931 steps required for synthesis. The original model is now in the Smithsonian Institution. The concept and development of this technique led to the award of the Nobel Prize in Chemistry to Dr. Merrifield in 1985.

45A An early model of the solid phase peptide synthesizer. The reaction vessel and liquid handling system is on the right and the stepping drum programmer is on the left. Designed and constructed by Bruce Merrifield, John Stewart, and Nils Jernberg, 1965.

46 Bausch & Lomb dissecting microscope especially built in 1920 with a stage mounted on a rotating ball for inspection, at all angles, of bacterial colonies growing on Petri dishes. Used by Dr. John Nelson.

47 Glass Kipp generator designed to produce gases for laboratory work. Used by Dr. P. A. T. Levene in the early 1920s, a time when compressed gases, such as sulfur dioxide, were not readily available commercially.

48 Specific gravity balance, circa 1920, used by Dr. Donald D. Van Slyke, especially for preparing different concentrations of copper sulfate. The red cells of healthy blood donors could be determined at once by adding one drop of blood to each cylinder of copper sulfate, since unhealthy cells were less dense.

49 Glass desiccator purchased from Germany in 1920. Dr. P. A. T. Levene's name is etched on the cover. The desiccator, for drying biological substances, has a built-in well in the cover to hold the moisture-absorbing agent, undiluted sulfuric acid.

50 Spencer dissecting microscope, about 1920, used by Dr. Clara J. Lynch for study of tumor-bearing mice.

51 Hand press for cutting tissue, shown disassembled.

Items 52A and 52B have been withdrawn.

52C Claude-Blum Ultramicrotome No. 2, developed here before 1947. This instrument was the first to allow continuous motion of the tissue block, and collection of sections on water for unfolding. Taken to Bruxelles in 1949 and there modified, it was returned in 1976 as an historical instrument. The pictures are originals, prior to modification.

A. Embedded tissue seized in a chuck.
B. Steel knife (B1) and water chamber (B2).
C. Lever (C1) to engage the pawl (C2) to start advancement.
D. Mechanical advance mechanism.
E. Thumb-actuated cogwheel for lining up the blade.
F. Wheel sizes varied for different cutting speeds.
G. Rod for removing mount carrying the block.
H. Oil cups.
I. Spotlight for oblique illumination.
J. Binocular low-power microscope for viewing sections.

52D Porter-Blum Ultramicrotome, mechanical advance, as used by Dr. Albert Claude. Designed at The Rockefeller University in 1951 by Dr. Keith Porter and Mr. Josef Blum (and built by Mr. Blum), this instrument opened a new era in electron microscopy. Examination of single cells by electron microscope became possible through Dr. Porter's practice of allowing explanted cells to grow as a monolayer over perforated grids (copper electromesh) coated with formvar film. Structures lying over the holes could be studied with the electron microscope. A parallel examination of tissues re-

quired extremely thin sections. The Porter-Blum ultramicrotome can cut sections of 50 to 100 millimicrons (5 to 10 thousandths of a millimeter) and, like the Ultramicrotome No. 2 (item 52c), made possible the cutting of ribbons of serial sections. Tissue was fixed and embedded in methacrylate plastic and seized by the chuck at the left of the long horizontal rod. A sharp glass knife, broken from 1/4-inch plate glass with pliers, was held in the adjustable cylindrical holder. One slow pass of the block against the knife severed a section of plastic, which was examined by a dissecting microscope mounted on the flat movable plate. If color (and therefore thickness) was satisfactory, a ribbon of consecutive sections was cut and individual sections were mounted on formvar-coated grids (like those displayed) for examination by EM. Each upward return of the arm and block was guided away from the knife by the offset gate.

A. Embedded tissue seized in a chuck.
B. Yoke, with double pivots.
C. Guide for arm, which cuts on downstroke.
D. Vise for glass knife (D1) with attached "boat" of water (D2).
E1. Loop handle engaging base of yoke with advance mechanism.
E2. Advance lever to set the rate of advance.

Early Micromanipulators.

These three are from Dr. Robert Chambers' items in the collection of Dr. Elaine G. Diacumakos, presented to the University by her husband James Chimonides.

Dr. Chambers (1881–1957) held positions at Cornell Medical and New York University at Washington Square.

53 Micropipette holder for attachment to microscope stage, improved over the first micromanipulator of Dr. Marshall A. Barber. The principle is the spreading apart, by thumbscrews, of clamped square brass rodding. (1921) *Science.* 54:411.

54 Left-handed micromanipulator for clamping to microscope stage or to an independent stand. Two are used, with different pipettes. (1922) *Journal of Infectious Diseases.* 31: 334–343.

55 Baseplate for clamping microscope, with service post and an attached syringe for microinjection. Two micromanipulators, as in 54 above were attached to the microscope stage. (1922) *Anatomical Record.* 24:1–23.

The Scientific Instruments Exhibition, which opened March 1, 1976, on the occasion of the University's 75th Anniversary, was planned and designed by Mrs. Patricia Berlin, Dr. Merrill W. Chase, and Mr. Fulvio Bardossi.

Fourth edition