NASA Grant NGL 14-001-012

Semi-Annual Progress Report

Period: May 1, 1968-October 31, 1968

H. Fernandez-Moran, M.D., Ph.D.
Department of Biophysics
The University of Chicago

Semi-Annual Progress Report

NASA Grant NGL 14-001-012

Title of Project: Investigations in Space-Related Molecular Biology Including Considerations of the Molecular Organization in Luster Sounding Rocket Program.

Period of Project: May 1, 1968 through October 31, 1968

Institution: The University of Chicago

Principal Investigator: Humberto Fernandez-Moran, M.D., Ph.D.
Professor of Biophysics
Department of Biophysics

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Principal Investigator
Dr. Humberto Fernandez-Moran

Grant Number
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Institution
The University of Chicago

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October 31, 1968

Title of Project
Investigations in Space-Related Molecular Biology Including Considerations of the Molecular Organization in Luster Sounding Rocket Program.

Our activities during this six-month period were carried out according to the program set forth in our renewal proposal and include:

I. Specific Research Program.

A. Continued Participation in the Luster Project and Related Projects for Electron Microscopic and Electron Optical Analysis and Identification of Extraterrestrial Matter:

Investigations have continued on the different size particles found (dense irregular, dense fluffy, and submicroscopic), confirming and extending results obtained from preliminary studies of the specimens, in 1965-66.

Attempts are being made to identify the amorphous electron sensitive material and other components found in association with these particles, by low-temperature electron microscopy and electron diffraction.

We are continuing to develop procedures for more precise and non-destructive examination of the particles with ultramicrotomy, using a diamond knife, and by high-resolution high-voltage electron microscopy and electron diffraction.

B. High-Voltage Electron Microscopy:

After careful preparations, we have installed a 200 kV electron microscope (Perkin-Elmer Hitachi Model HU-200E) which was built to our specifications, providing exceptionally high voltage regulation (in the order of 1 to 2 parts per million at 200 kV) and objective lens current regulation (1 to 1.5 parts per million over 2 to 3 minute periods, as determined by precise measurements carried out in our labs with exceedingly low ripple).

This instrument, which we believe is the first of its kind used for biological work in this country, has been installed in a special room with minimum magnetic, electrical, and mechanical perturbations, and provided with a highly regulated main power supply (separate motor generator set with solid state regulator, guaranteeing constant voltage with very low harmonic distortion).

Under these optimum conditions, we have achieved resolutions of 3.6Å to 6Å in crystalline lattices, and of about 4Å point-to-point resolutions in thick (about 250Å to 350Å) biological specimens. We believe that this represents the highest resolution yet achieved at 200 kV.

The combination of high resolution with decreased radiation damage to organic specimens is quite remarkable. Although our work is still in a preliminary stage, we anticipate significant advantages in the study of relatively "thick" biological specimens.

Since the ratio of phase contrast to specimen damage for constant exposure improves and reaches a maximum at about 200 kV, as pointed out by Heidenreich (Jap. J. Electr. Micros., Vol. 16, 1967, p. 38), we believe that this approach offers unique advantages in the study of biological ultrastructure.

We are currently adapting pointed filaments with cathode caps of special design to obtain enhanced contrast in combination with improved ultra-miniaturized phase contrast, thin-film zone plates, of the type already described in our papers at the Sixth International Congress for Electron Microscopy at Kyoto, Japan in 1966. This should prove to be of particular value in the study of wet or hydrated biological specimens enclosed in the special type of vacuum-tight microchambers which have been further refined since we introduced them in 1960.

C. <u>High-Resolution Low-Temperature Electron Microscopy of Biological Systems</u>:

We are presently installing and adapting to our facility a closed-cycle superfluid liquid helium refrigerator system, developed by Professor Samuel Collins, A. D. Little, Inc.

This unit is the first of its kind in the world and when in successful operation will permit us to work continuously in the low-temperature range of 1.85° to 2.0°K. Prior to shipment, the unit was tested by A. D. Little, Inc., running successfully at 1.8°K with 20 watts refrigeration capacity, representing the highest performance yet achieved in the cryogenic field.

We will soon be able to operate the 200 kV electron microscope at liquid helium and liquid nitrogen temperatures, thus gaining access to a whole new domain of ultrastructural investigations.

D. <u>Improved Instrumentation and Preparation Techniques for High Resolution Electron Microscopy</u>:

Continued developments have centered on:

1) improved point cathode sources with single-crystal filaments and new thin film molybdenum gun design,

2) short focal length objective lenses with improved stability,

3) high-resolution phase contrast imaging with zone-plate apertures of precise shape, which have been produced by special microengraving methods developed in our laboratory,

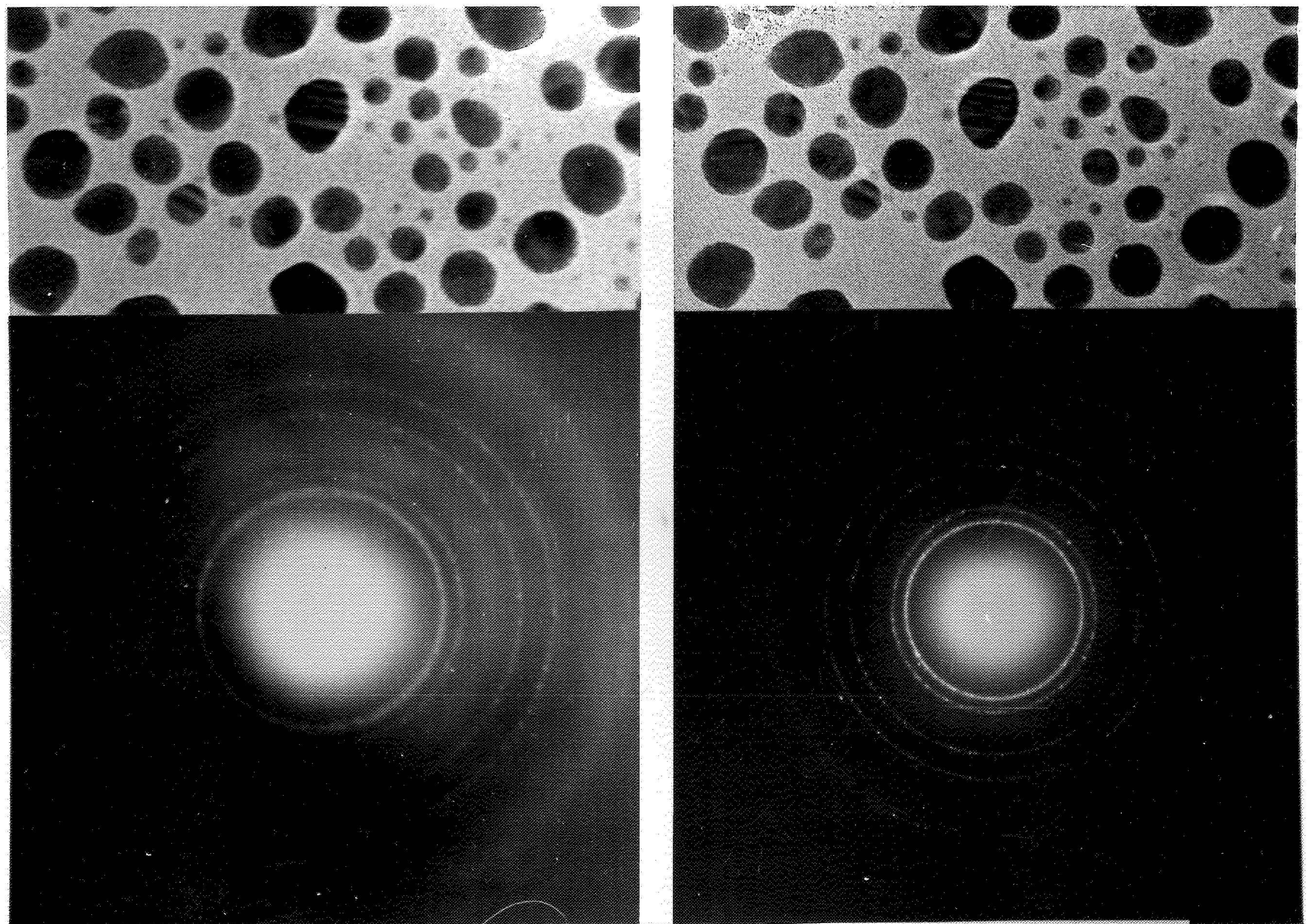
4) high-resolution electron optical demagnification and recording on special thin film substrates

5) electron microscopy with superconducting lenses operating at liquid helium temperatures.

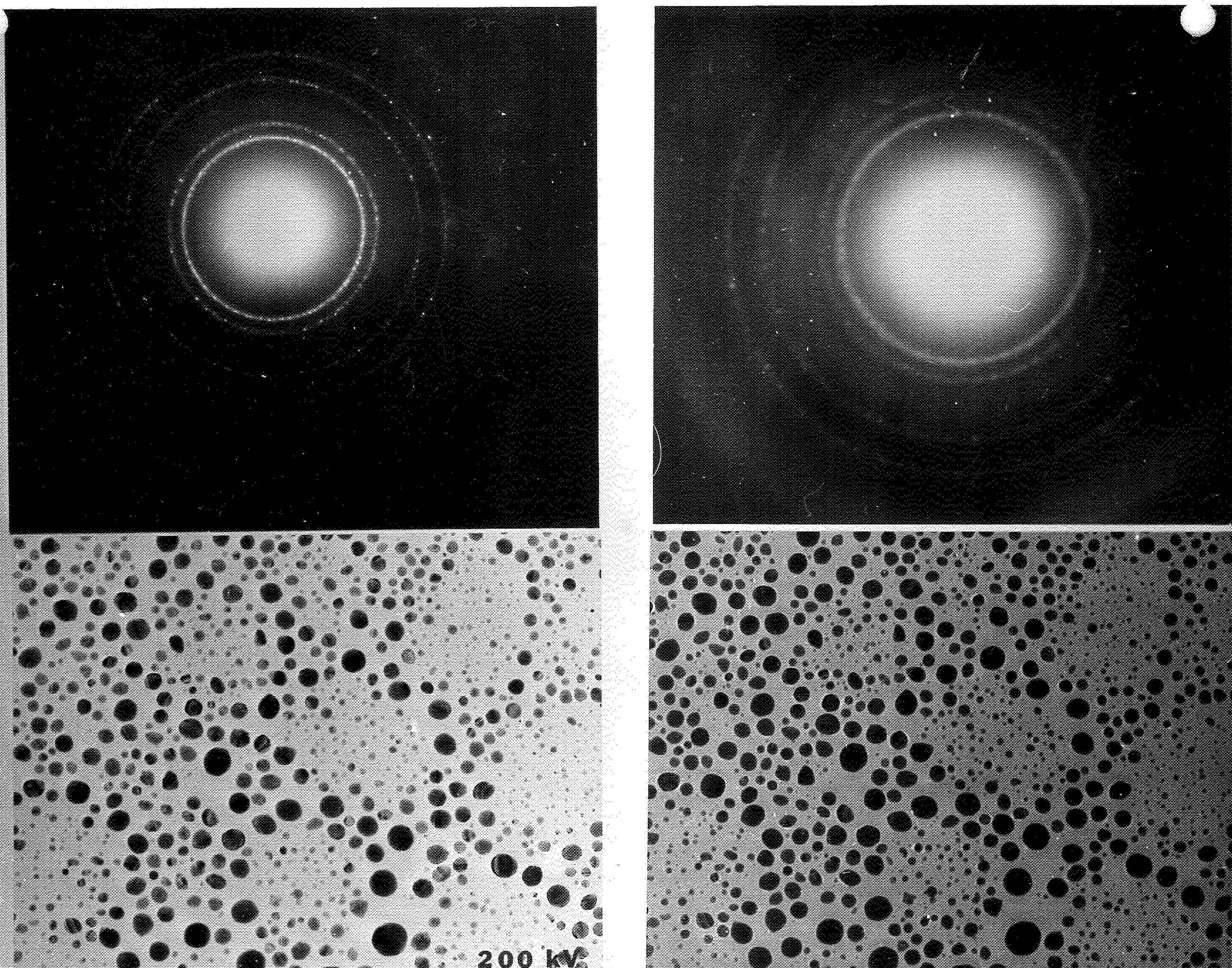
II. <u>Publications and Supporting Material for the Period May 1, 1968 through October 31, 1968</u>.

1. H. Fernandez-Moran, "The World of Inner Space," Science Year 1968, THE WORLD BOOK ENCYCLOPEDIA SCIENCE ANNUAL, p. 216.

2. H. Fernandez-Moran, "Humanity and Science at the Crossroads," keynote address presented at the banquet of the National Conference on Industrial Research and I-R 100 Awards Program, October 4, 1968.



COMPARISON ELECTRON MICROGRAPHS AND SELECTED-AREA ELECTRON DIFFRACTION PATTERNS OF SUBMICRON PARTICLES, PRESUMABLY OF EXTRA-TERRESTRIAL ORIGIN OBTAINED DURING THE LEONID (1966) ROCKET SOUNDING EXPERIMENTS (ALTITUDE APPROXIMATELY 140 KILOMETERS). THE GREATER PENETRATION POWER OBTAINED WITH THE NEW 200 kV ELECTRON MICROSCOPE (RIGHT) SHOW CHARACTERISTIC FEATURES WHICH ARE NOT CLEARLY VISIBLE WITH THE STANDARD 100 kV INSTRUMENT (LEFT). ELECTRON DIFFRACTION PATTERNS AND HIGH-RESOLUTION ELECTRON MICROGRAPHS ARE VERY SIMILAR TO THE Fe-Ni ALLOYS (TAENITE AND KAMACITE) OBSERVED IN OTHER MICRO-METEORITE PARTICLES. THE HIGHER PENETRATION POWER AND REDUCED SPECIMEN DAMAGE OF HIGH VOLTAGE ELECTRON MICROSCOPY OFFERS PROMISING NEW APPROACHES TO THE STUDY OF EXTRA-TERRESTRIAL PARTICLES.
(Micrographs recorded at high resolution electron microscopy facility of the University of Chicago, Dr. H. Fernandez-Moran)



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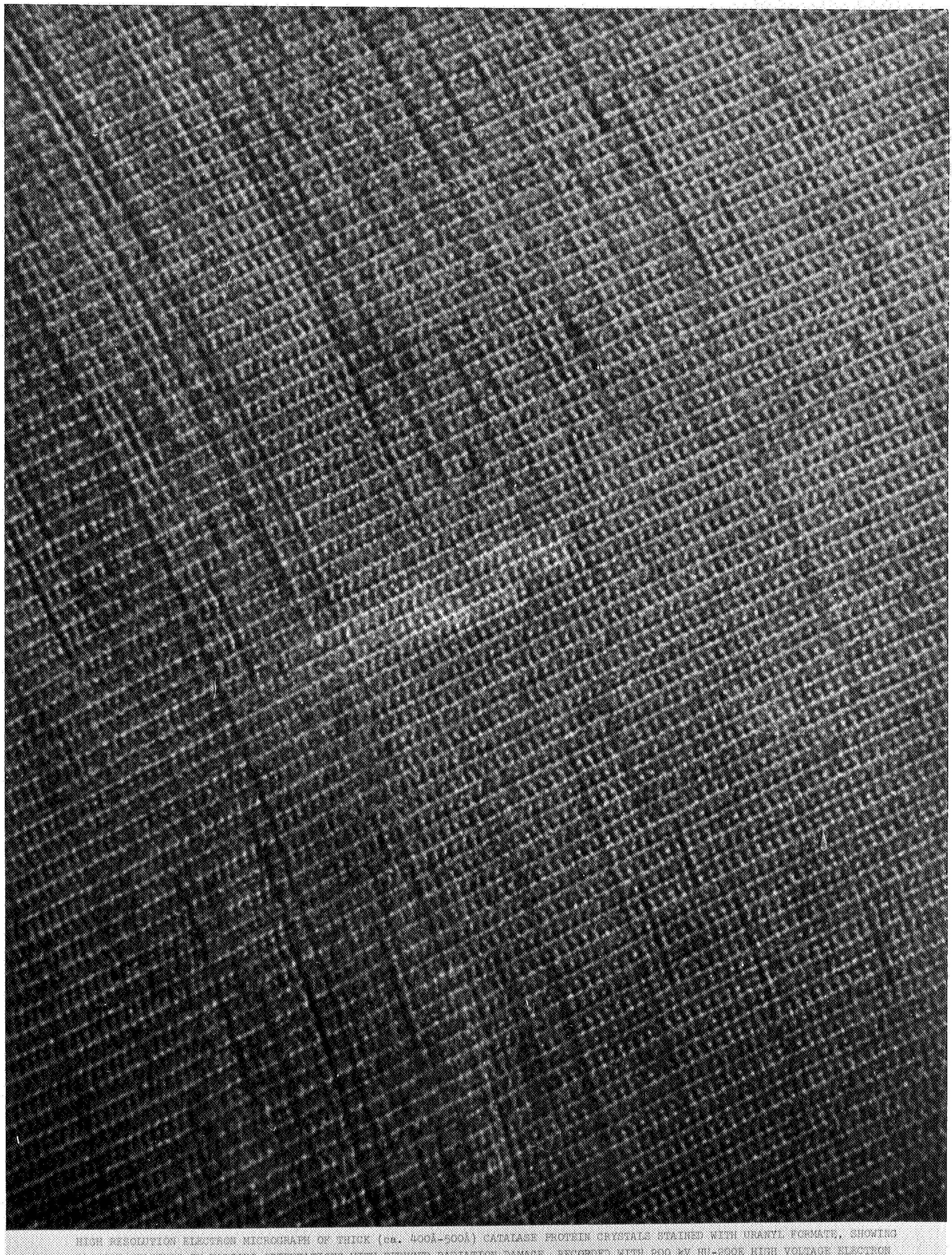

HIGH RESOLUTION ELECTRON MICROGRAPH OF THICK (ca. 400Å-500Å) CATALASE PROTEIN CRYSTALS STAINED WITH URANYL FORMATE, SHOWING LATTICE SPACINGS IN VARIOUS ORIENTATIONS WITH REDUCED RADIATION DAMAGE, RECORDED WITH 200 kV HU-200E HIGH VOLTAGE ELECTRON MICROSCOPE PROVIDED WITH HIGHLY STABILIZED CENTRAL POWER SUPPLY. (Electron Microscopy by M. Ohtsuki, Photography by Charles Hough, Laboratory of Dr. H. Fernandez-Moran, University of Chicago)

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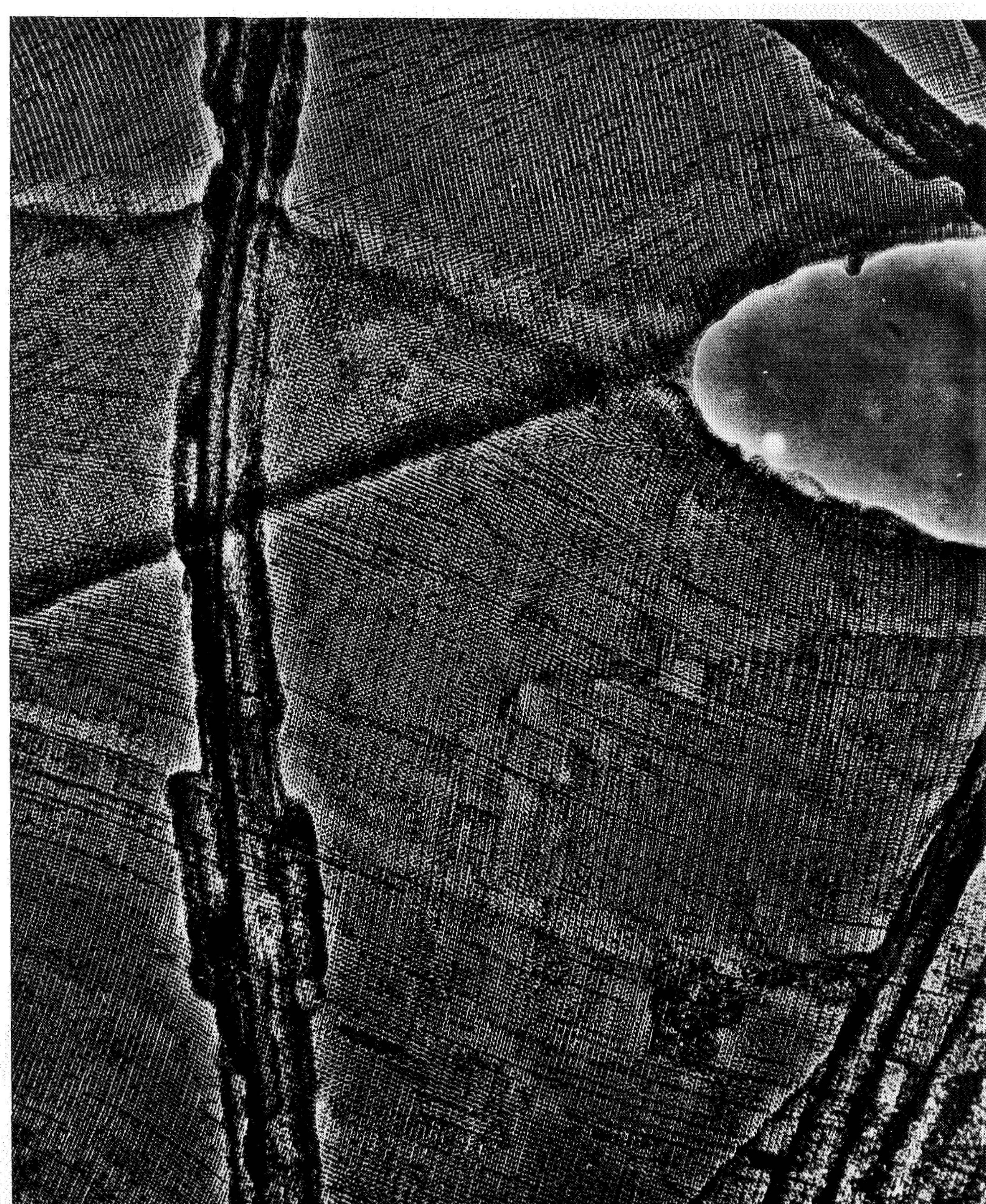

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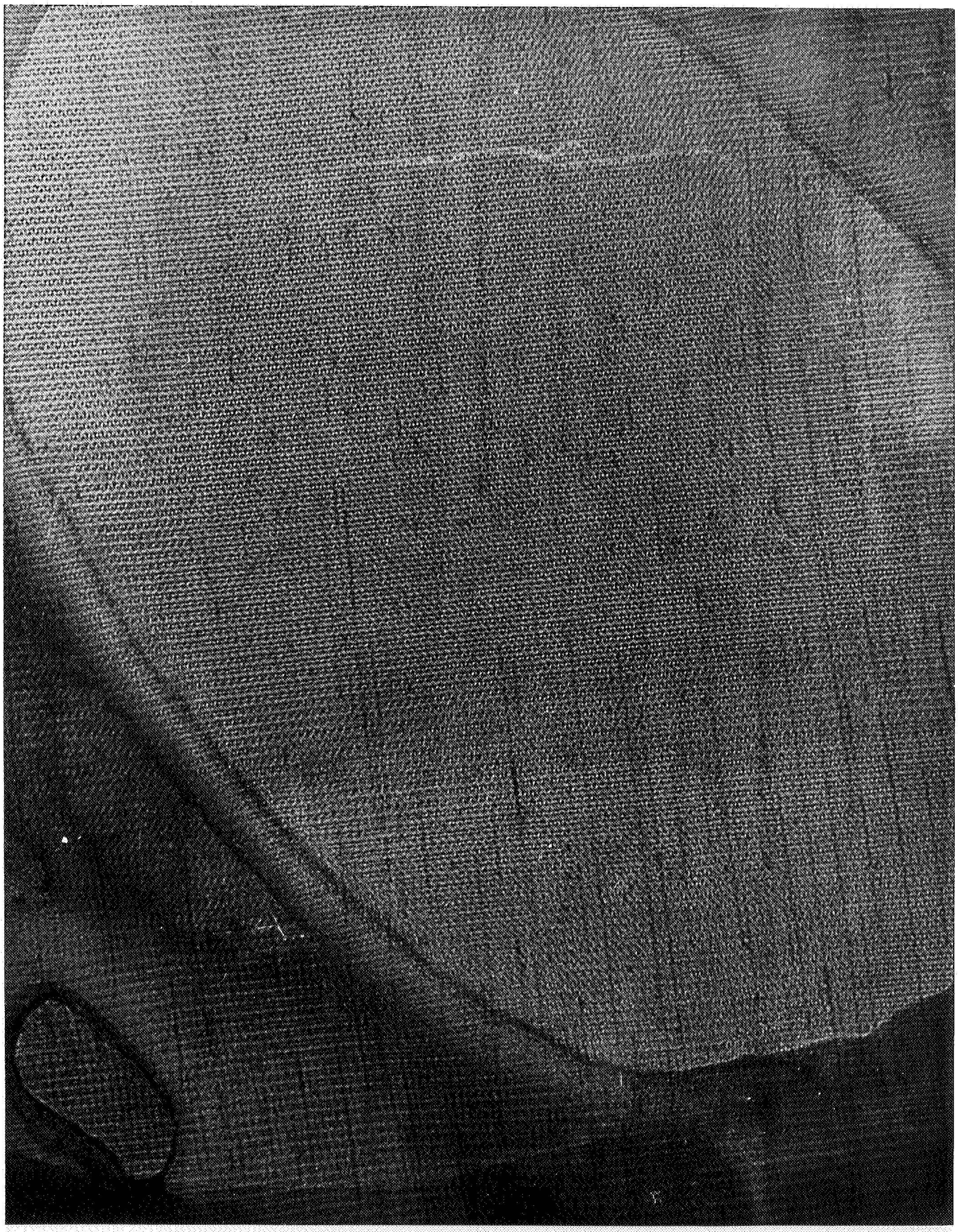

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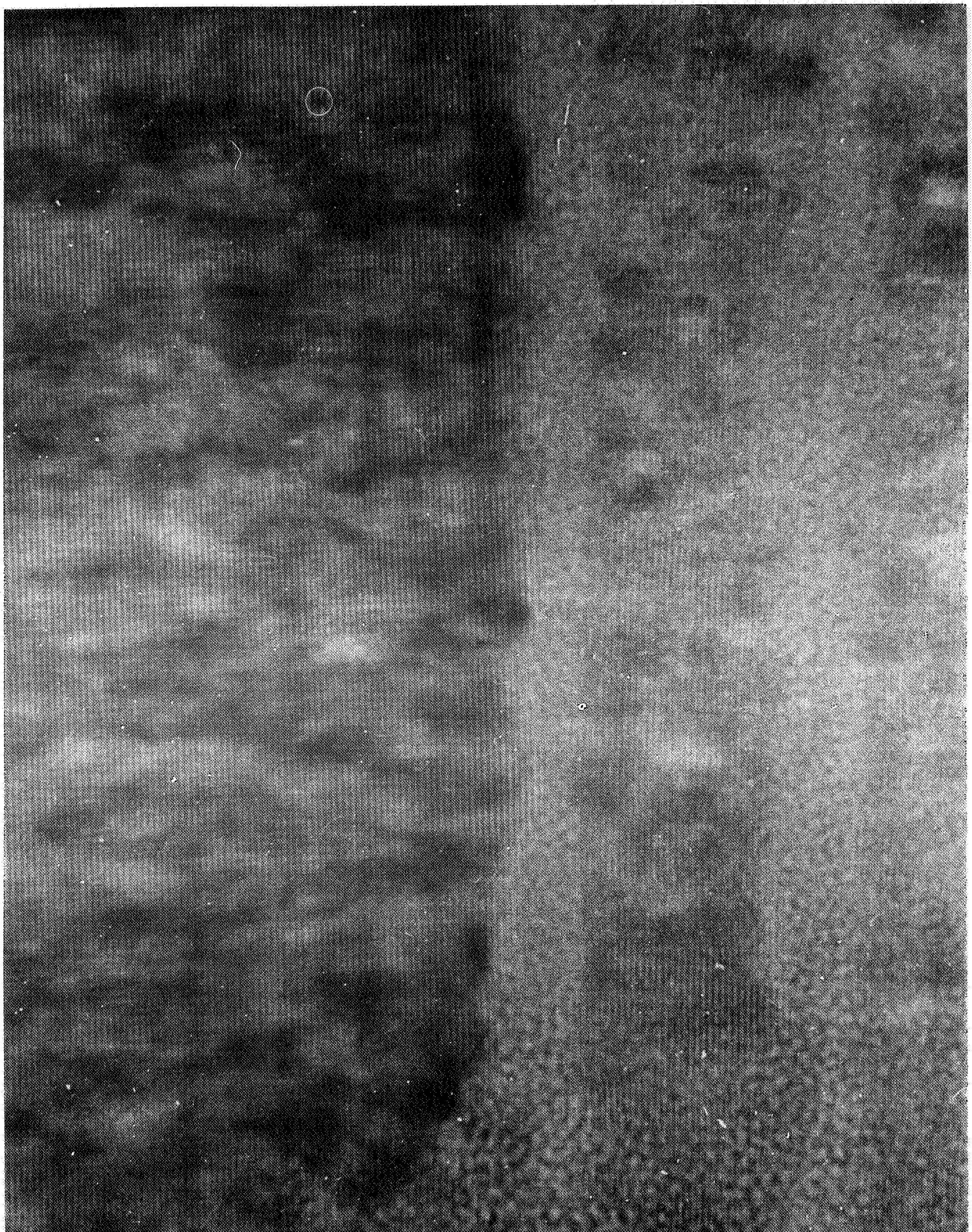
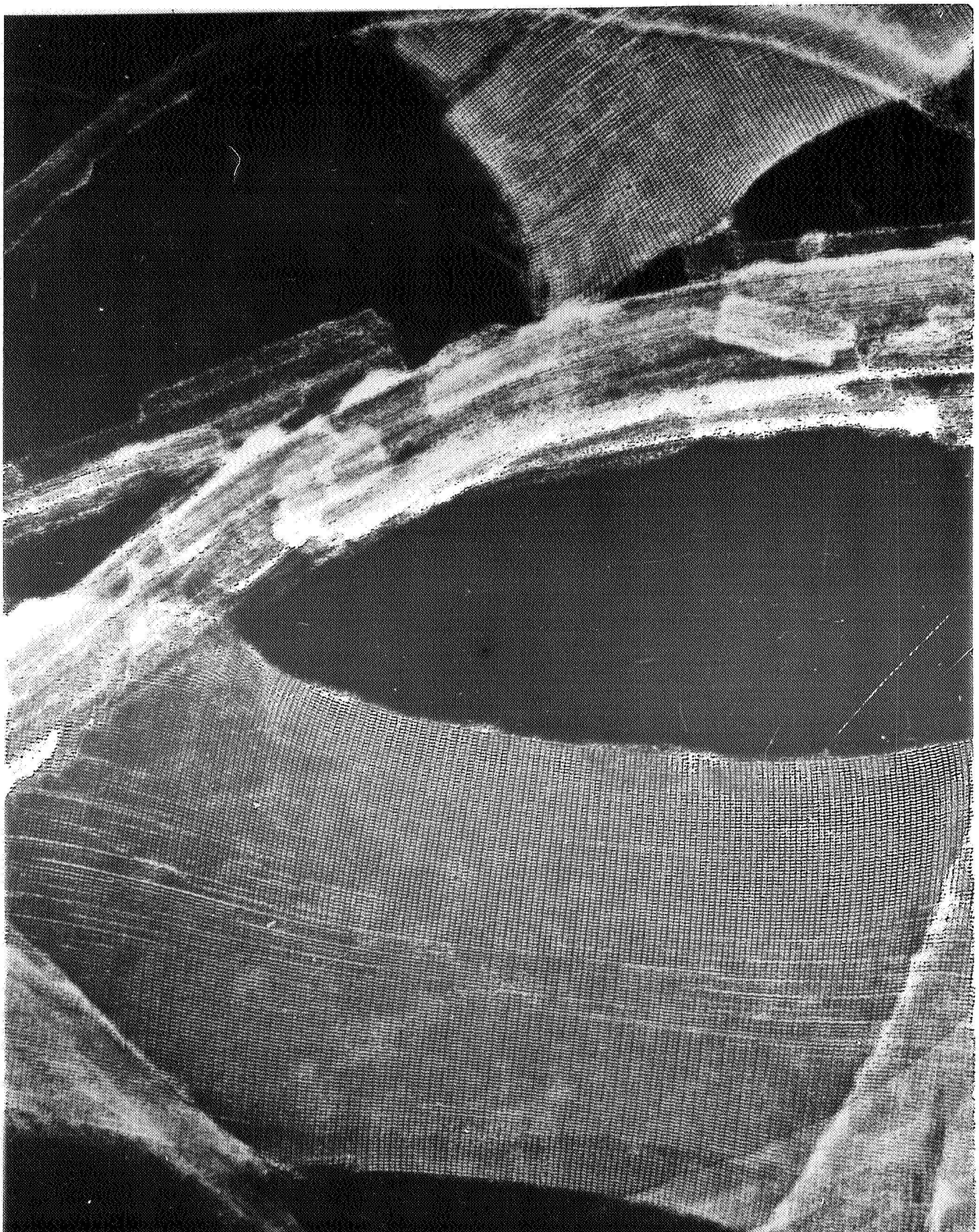


HIGH RESOLUTION ELECTRON MICROGRAPH OF THICK (ca 250Å) SINGLE CRYSTAL LAYER OF K_2PtCl_4 SHOWING 6.94Å LATTICE SPACING. RECORDED WITH 200 kV HU-200 E HIGH VOLTAGE ELECTRON MICROSCOPE PROVIDED WITH HIGHLY STABILIZED CENTRAL POWER SUPPLY. (Electron Microscopy by M. Ohtsuki, Laboratory of Dr. H.Fernandez-Moran, University of Chicago) MAGNIFICATION: 3,200,000 X.



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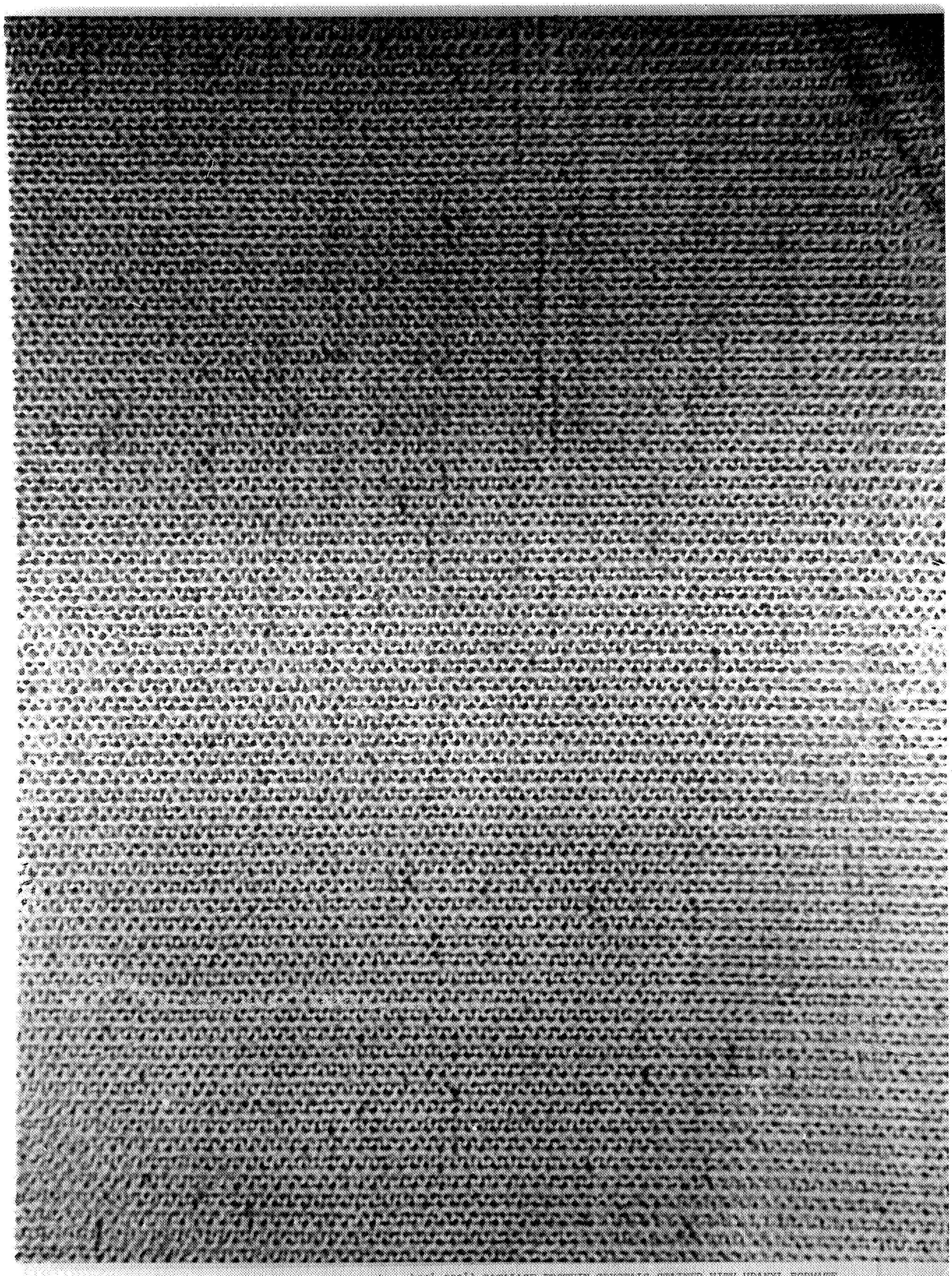

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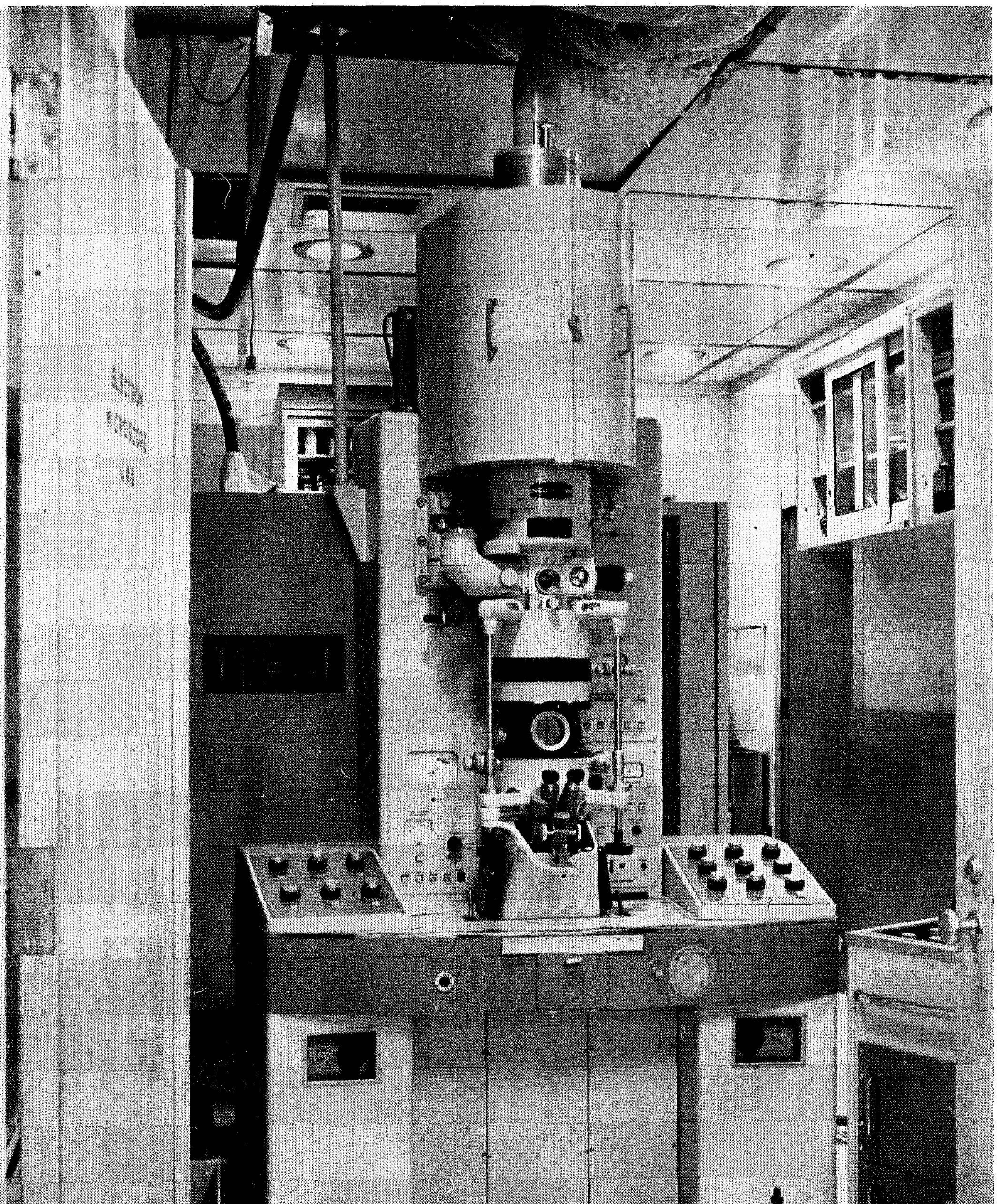
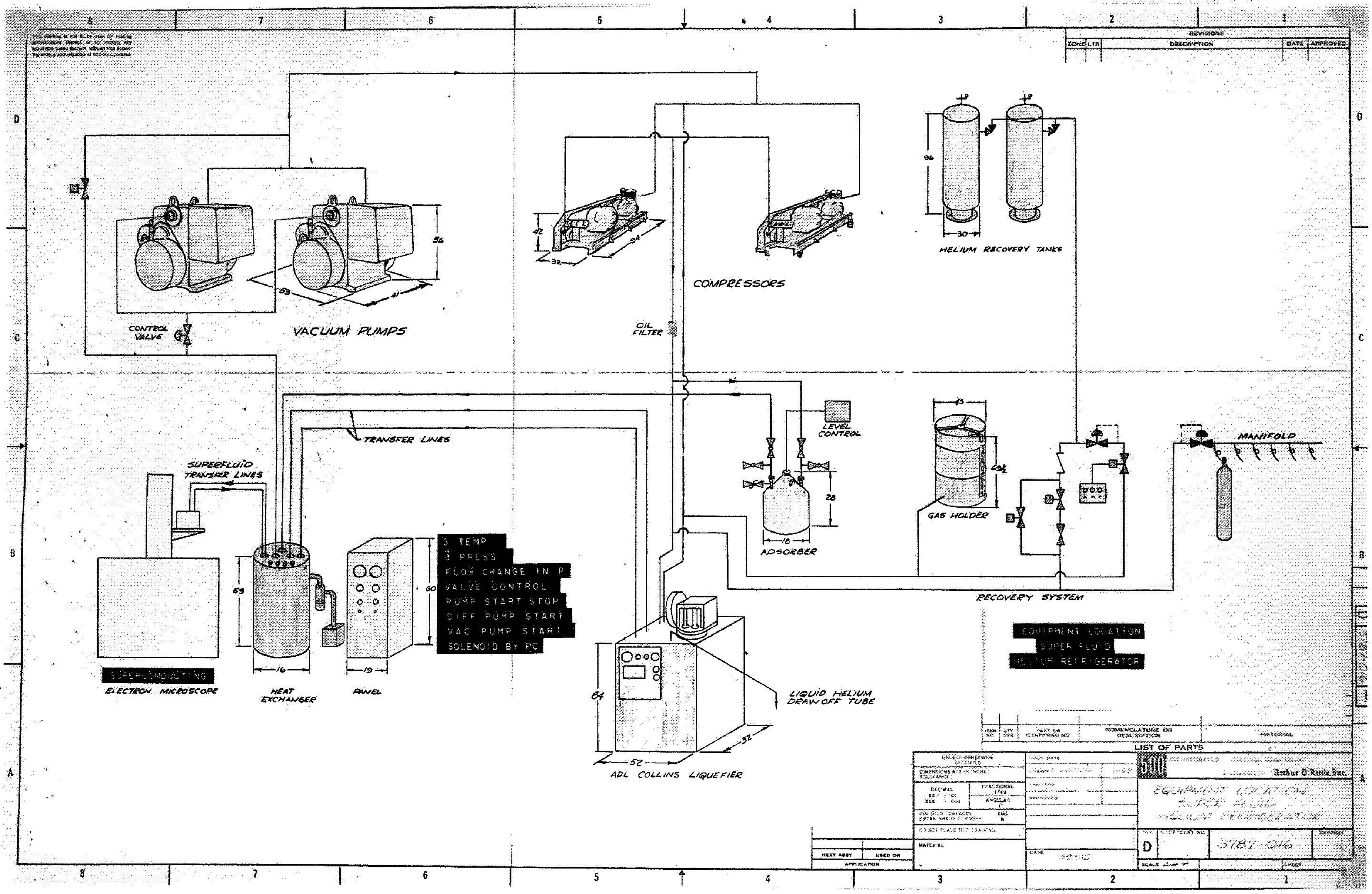


NEW 200,000 VOLT HIGH RESOLUTION ELECTRON MICROSCOPE (HU-200E), SPECIALLY INSTALLED AND PROVIDED WITH HIGHLY STABILIZED CENTRAL POWER SUPPLY AT THE ELECTRON MICROSCOPE FACILITY, DEPARTMENT OF BIOPHYSICS, UNIVERSITY OF CHICAGO, SEPTEMBER, 1968. THIS INSTRUMENT, WHICH IS THE FIRST OF ITS KIND INSTALLED IN A BIOLOGICAL LABORATORY, GIVES HIGH PENETRATING EFFICIENCY, LOW SPECIMEN DAMAGE, HIGH DIFFRACTION ACCURACY AND LOW CHROMATIC ABERRATION.


VACUUM PUMPS
CONTROL VALVE
COMPRESSORS
OIL FILTER
HELIUM RECOVERY TANKS
TRANSFER LINES
SUPERFLUID TRANSFER LINES
LEVEL CONTROL
ADSORBER
GAS HOLDER
MANIFOLD
RECOVERY SYSTEM
3 TEMP
3 PRESS
FLOW CHANGE IN P
VALVE CONTROL
PUMP START STOP
DIFF PUMP START
VAC PUMP START
SOLENOID BY PC
SUPERCONDUCTING ELECTRON MICROSCOPE
HEAT EXCHANGER
PANEL
LIQUID HELIUM DRAW OFF TUBE
ADL COLLINS LIQUEFIER
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LIST OF PARTS
Arthur D. Little, Inc.
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The World Book

Encyclopedia

Will it someday be possible to build the brainlike machine that Warren McCulloch envisioned? Perhaps, even without the extreme miniaturization that Feynman suggests. Some experts, for instance, count on scientific and engineering genius to create a multitude of "functional circuits." According to Jack Morton, who directed the transistor into a practicable device at Bell Telephone Laboratories, designers are still thinking conventionally, in terms of individual circuit parts acting together. Functional circuits of the future would, however, have no recognizable parts that could be identified as, for example, a transistor. Instead, a special material would be processed to perform an elaborate function, such as the coding of spoken messages into dots and dashes.

The functional vanguard

A few functional devices do exist. A familiar example is the quartz crystal in a phonograph pickup that converts mechanical vibrations into a varying electric current. Another functional circuit is the laser. It does what no ordinary assemblage of electronic parts can accomplish in absorbing random energy and emitting light waves of a specific frequency that are precisely in step with one another.

Henry Zimmerman, director of M.I.T.'s Research Laboratory of Electronics, is optimistic about yet another approach. He points out that the Hungarian-American mathematician John von Neumann worked out a general theory for building highly reliable machines from unreliable parts. Such a machine would, in principle, perform much like a brain, which works remarkably well with its erratic nerve cells. Zimmerman explains that only up to a point does an increase in the complexity of a machine reduce its reliability. Beyond this point, with more circuits, machines can take advantage of a different principle. The brain seems to be a parallel machine; it works on a great many tasks at the same time. Up to now, computers have been sequential; they complete one task before starting the next. Using the speed and reliability of ICs that will be available a few years from now, it may be possible to design information processors that are organized in a parallel fashion.

Zimmerman, like most scientists, doubts that man will soon reproduce his brain in electronic hardware. But, using a multitude of ICs, ultraminiaturized, working in parallel, together with functional circuits, he may build electronic devices tomorrow that seem like impossible dreams even today.

For further reading:

"Gulliver-Size Need for Lilliputian Products," *Time*, Sept. 2, 1966.

Hittinger, William C., and Sparks, Morgan, "Microelectronics," *Scientific American*, November, 1965.

"Hookup to the Future," *Business Week*, Nov. 4, 1967.

A Science Year Report

By Humberto Fernandez-Moran

The World of Inner Space

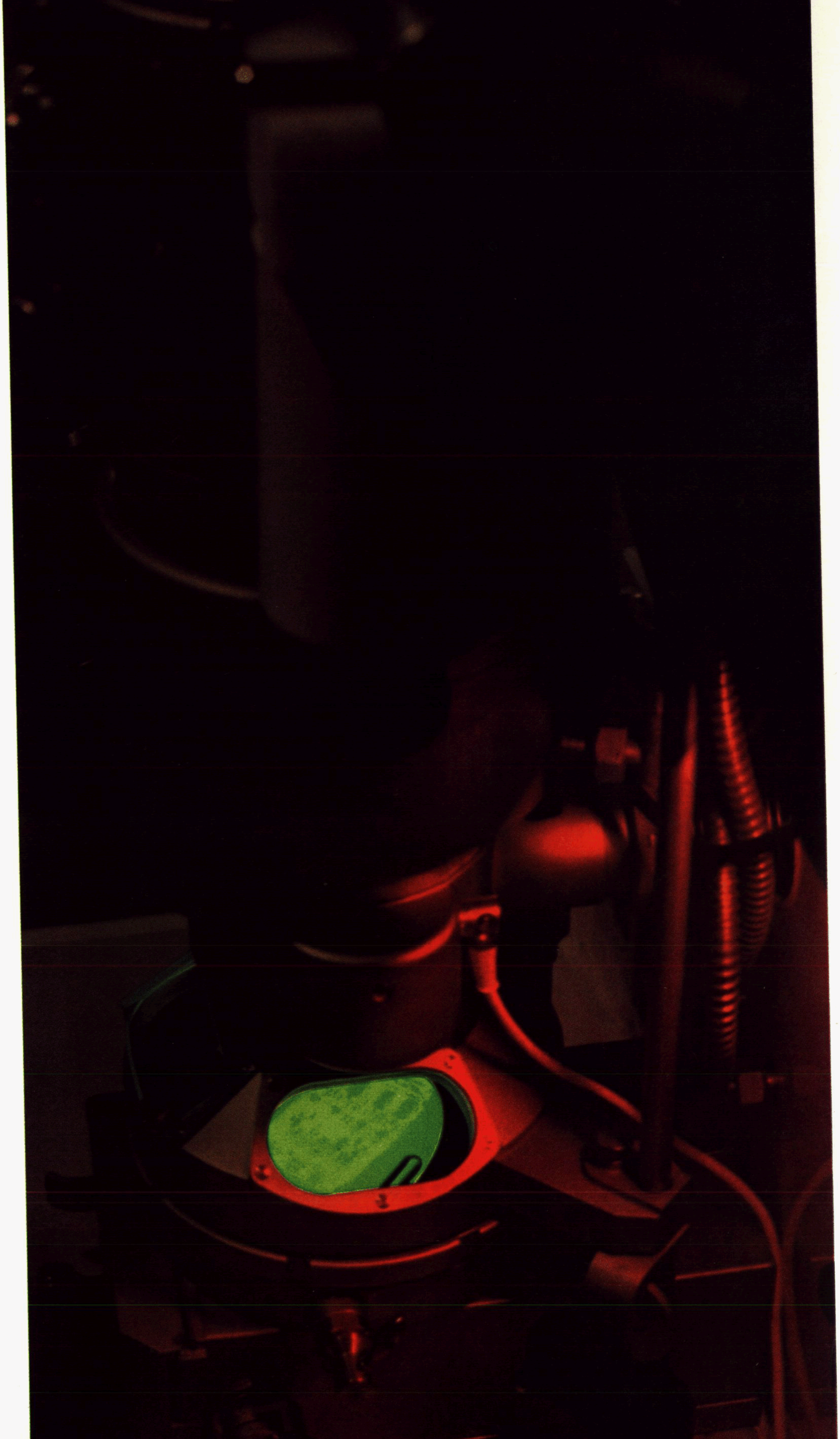
With the electron microscope, man is beginning to discover the secrets of atoms and molecules, and may soon be designing matter at this level

Man is exploring a new universe, inner space–through a powerful and promising instrument, the electron microscope. As does his counterpart, the astronomer, the electron microscopist is using his technology to overcome the limitations of his eyes. And, like the astronomer, he is attempting to find order and meaning in the world of the infinite he observes.

But the electron microscopist has one great potential advantage. An astronomer can only observe the planets, the stars, and the galaxies. The microscopist, however, not only can look into his magnified world of atoms and molecules, but may soon begin to manipulate it. For example, he may someday be able to alter the molecules that determine man's genetic makeup and correct molecular defects. He can also use the device like an inverted telescope, to condense massive libraries onto a single page, or print electronic circuits the size of red blood cells to transmit information from within the human body.

To understand the significance of the electron microscope, we need to understand the principles of magnification. We see an object because light waves carry its image to our eyes. In examining the object

In the eerie green glow of electron microscope viewing ports, scientists observe specimens with a spectacular degree of magnification and detail.



in detail, we bring it closer to our eyes to spread out its features and make it appear larger. However, we cannot focus on objects less than about 10 inches from our eyes. We must then use an external lens, such as in a magnifying glass, to further spread the features.

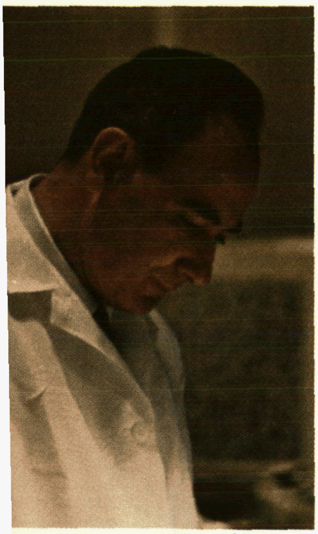
The optical microscope, which extends this principle, is basically a system of glass lenses used in conjunction with a source of concentrated light that illuminates the object to be viewed. Optical microscopes have been developed to a point where they can magnify an object up to 2,000 times, and at the same time resolve features on it only 2,000 angstroms (A) apart (one A equals 1/100,000,000 centimeter, or about the diameter of an atom). This is about the limit of optical microscopes because of the nature of light and distortions inherent in the lenses. The central problem is that it is impossible to resolve points on an object that are closer together than the length of the wave that is carrying the image.

This limit was breached with the development of the electron microscope a little over 30 years ago. The unique properties of electrons–they are both electrically charged particles and waves–permit them to be focused like light. Because electron waves are several hundred thousand times shorter than light waves, they can resolve much smaller objects. Today's electron microscopes can, in practice, resolve points on an object only 5 A apart, while magnifying the object as much as 1 million times.

In the conventional electron microscope, the source of illumination is electrons, and the lenses are electromagnetic fields existing in a vacuum. A beam of externally generated high-voltage electrons enters the microscope through a tube at the top. After being concentrated by a condenser lens, it passes through the specimen to be viewed. This scatters the electrons, which are then formed into an image by passing through a series of focusing lenses. The beam finally arrives at a fluorescent screen near the bottom of the microscope where the electronic image is converted into a visual image. This greatly magnified image is viewed through an observation window.

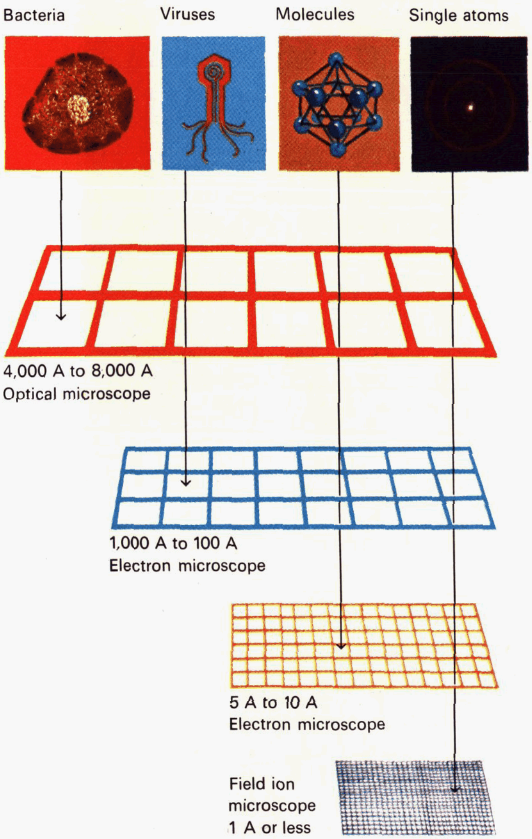
The electron microscope is a highly versatile instrument. Its illumination can be varied from a few to several million electron volts, and the lenses can be focused over a wide range. This versatility promises to let us look even farther into the world of atoms and molecules. To push back the frontier, however, we must make improvements in three major areas: (1) in the environment of operation, (2) in our instruments, and (3) in our preparation techniques.

Because electron microscopes are extremely delicate, they are adversely affected by many external factors. Chief among these are electromagnetic interference, vibration, and contamination. We have gone to great lengths to minimize these factors at our nine-microscope laboratory at the University of Chicago. For example, to reduce electromagnetic disturbances, we use incandescent rather than fluorescent lights. Also, all the electrical wiring is shielded in grounded conduits behind the walls. Even the ventilator ducts are made of nonmagnetic stainless steel.



The author:
A native of Venezuela, Humberto Fernandez-Moran holds an M.D. degree from the University of Munich, an M.D. from the University of Caracas, an M.S. in cell biology and a Ph.D. in biophysics from the University of Stockholm. He is one of the leading inventors and developers of electron microscopes and microscopy techniques.

What Microscopes Resolve



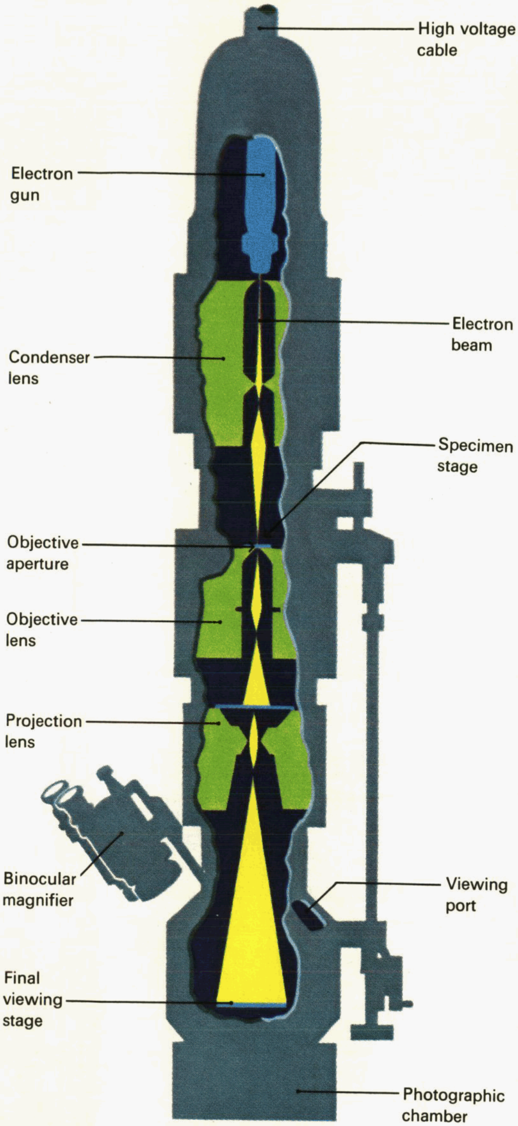
Resolution of points on an object is proportional to the wave length of the illuminating source. The best optical microscopes, resolving points 4,000 to 8,000 angstroms (A) apart, permit the viewing of bacteria. Depending on choice of magnification, conventional electron microscopes can show viruses in the 100 to 1,000 A range or groups of molecules at from 5 to 10 A. The special features of field-ion microscopes may provide a resolution of 1 A, or the diameter of a single atom.

To eliminate vibration, we mount the microscopes on individual concrete blocks that sit on springs in the floor and are insulated by shock pads. The contamination problem is met by having as dirt free a laboratory as possible. All who enter the air-conditioned laboratory must pass through a special anteroom where they stop to don white nylon coats. Employees wear special shoes and visitors are furnished plastic bags to wear over their shoes.

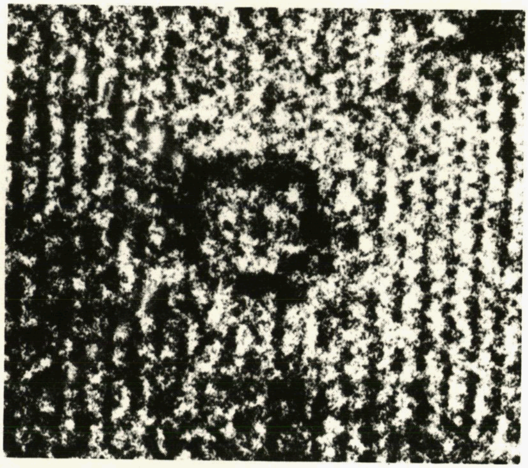
To improve the electron microscope itself, we must start with the elimination of lens fluctuation. All electronic systems are subject to thermal noise caused by hot electrons moving through the circuits. In an electron microscope, this noise causes variations in the focusing of the lenses. One way to solve this problem is to place the windings of the electromagnetic lenses in a very cold environment—that of liquid helium. At about 4.2°C. above absolute zero, the current goes into a state of superconduction; that is, the power may be turned off and the current will continue to flow without meeting electrical resistance. It thus sustains a very constant magnetic field.

Another avenue of instrument improvement is the development of high-voltage microscopes. Electrons are absorbed by very thin layers of matter. Therefore, specimen tissues must be sliced thin enough—

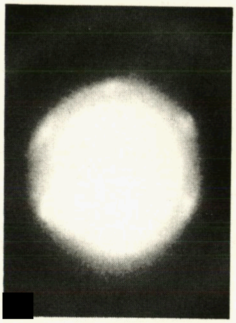
The Electron Microscope



In the electron microscope, specimens are illuminated by externally generated electrons that are beamed by an electron gun into an electromagnetic condenser lens. The concentrated beam passes through the specimen, which scatters the electrons. A series of lenses then focus the electrons into an image of the specimen and adjusts its magnification. A final lens projects the image on a fluorescent screen where it can be viewed directly or it can be photographed. The microscopes can be operated over a wide range of voltages and lens magnifications.

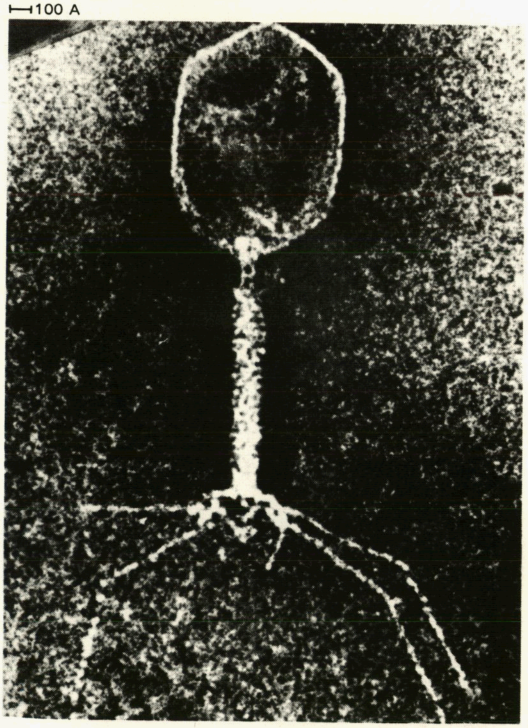


100 A



Special methods permit direct view of an organic molecule, *above,* coupled with electron diffraction of a selected area, *left,* to determine details between 2 and 3 A. The high resolution of a bacterial virus, *below,* portrays the structure of its head and tail.

100 A



from 50 to 100 A–so that most electrons can pass through them. Living systems, such as bacteria, are much thicker than this, and viewing them requires the more energetic high-voltage electrons. The primary advantage, however, lies in better resolution. As the voltage is increased, the wave length of the electrons becomes smaller. High-voltage microscopes now being developed provide resolution approaching 1 A.

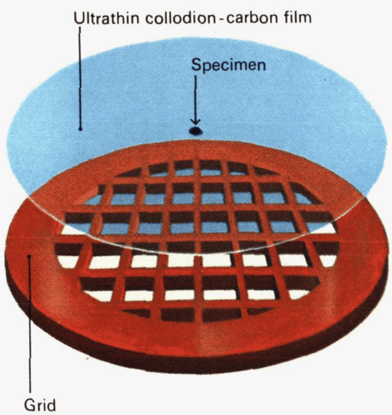
Another goal in our technology is the improvement of the electron beam itself. We would prefer a beam that is coherent—all the electron waves traveling in step with each other, like an army on parade. This not only would improve the resolution but, used in conjunction with superconducting lenses, would also make possible the technology of high resolution holography.

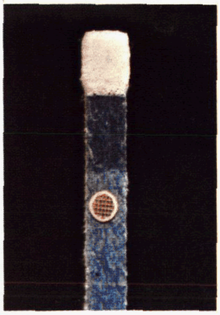
Holography is a method of recording images on film without a lens. It requires a coherent illuminating beam, divided so that one part lights the object, while the other, called the reference beam, goes directly to the film. At the film, the reference beam and the light from the object cause an interference pattern that contains all the information on the image in three dimensions. The scene can then be reconstructed by viewing the developed film with another coherent illumination source.

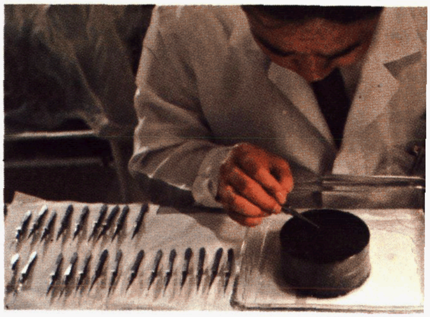
This imaging system was, in fact, first proposed by a scientist working with electron microscopes. In 1948, Dennis Gabor, a Hungarian physicist then at the University of London's Imperial College of Science and Technology, had come to believe that electromagnetic lenses could not be substantially improved. So he proposed taking magnified pictures with an electron microscope by exposing a photographic film to the electron waves from the specimen before they were focused, and reconstructing the jumbled image with visible light. Because light waves are much longer than electron waves, the reconstructed image would be greatly magnified.

With the invention of the laser, it became possible to make holograms using visible light. This device provides the coherent beam of

Holding the Specimen

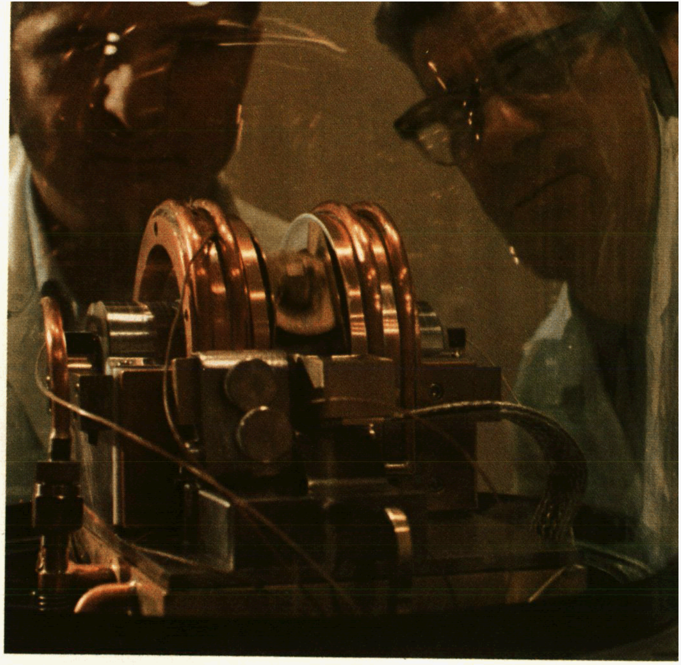






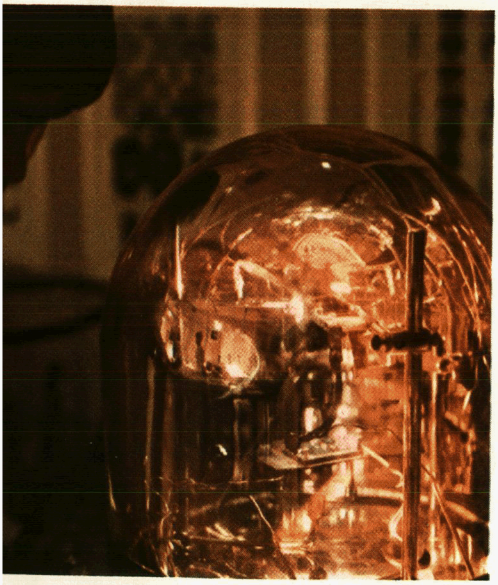
Specimens require special handling devices such as the grid, *left,* shown slightly enlarged, *above.* Laboratory technician, *right,* prepares ultrathin films used to support the specimens on the grids.

Scientists and technicians prepare specimens to be viewed through the electron microscope under conditions that approach operating room cleanliness.



A new cryogenic ultramicrotome is used to section frozen biological specimens.

Video recording system with image intensifier is a valuable tool for registering specimen behavior for large group demonstrations.



Thin layer of metal is deposited on specimens in ultrahigh vacuum, *left*. Photographic laboratory, *above*, includes shadowgraph on which projected image from the microscope can be studied in detail.

light necessary for the successful imaging and reconstructing of realistic three dimensional scenes. In the electron microscope, holography will reveal interatomic distances and show us structures in three dimensions. This application, however, must await the development of laserlike devices that will provide a coherent electron beam.

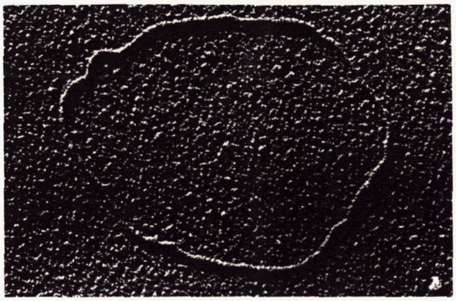
An interesting variation on conventional electronic microscopes is being developed by Albert Crewe, working with another group here at the University of Chicago. In this microscope, a highly concentrated electron beam is focused before reaching the specimen, and is then scanned across it. The electrons that pass through the specimen are collected and compared with those that are scattered. The energy lost by the traversing electrons can be used to identify the specimen. Thus the scanning electron microscope will be able to analyze a material while simultaneously observing its atoms and molecules. And, because the electron beam examines a smaller portion of a specimen at a time, it has a potential for much improved resolution.

Sharing importance with advances in the electron microscope are improvements in the techniques for preparing specimens. One of the most spectacular developments in this area has been a system for precisely slicing specimens into ultrathin sections. The system consists of a diamond knife operating in an evacuated microtome. It can be operated at very low temperatures in order to keep rearrangement of the molecules in biological specimens to a minimum.

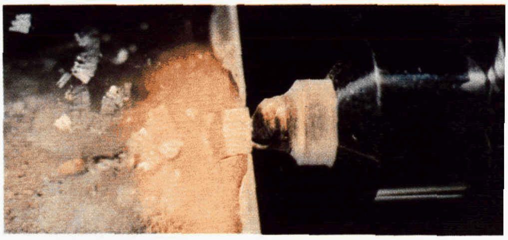
The idea for this system came to me while flying over Angel Falls in Venezuela. As I looked down on the beautiful cascading waters of the world's highest waterfall, I suddenly realized that our sectioning problem could be solved by a device that provided a precise, circular motion in a smoothly recurring flow system. The result was the invention of the ultramicrotome—a fine rotating slicing machine similar to a meat slicer.

Our precision machine needed an ultrasharp knife—sharper than anything available. I ruled out steel because of the limits to which it could be ground. Then I thought of diamonds. Because they are chemically inert, they would not contaminate organic specimens. But even better, I knew, from having studied diamonds under the electron microscope, that they are giant crystals composed of

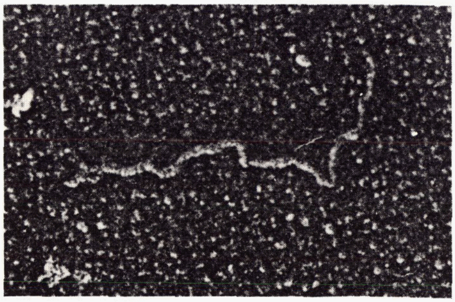
Editing the Code of Life



Closed strand of a virus DNA, *above*, can be seen in an electron microscope. After reaction with nucleotides and an RNA polymerase varying width filaments are formed, *below*.



The diamond knife, *above*, can cut large biological molecules into viable segments, such as a section of virus DNA, *below*. The technique may permit genetic defects to be corrected under the microscope.

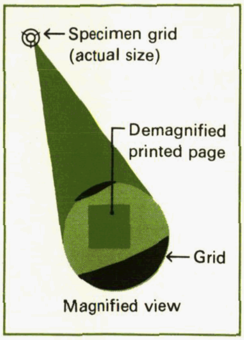


layers with atomically smooth knife edges. I began slowly and carefully to pare away the layers of a diamond with the only tool hard enough to do so—another diamond. After many hours of work, I was rewarded with the finest knife yet made.

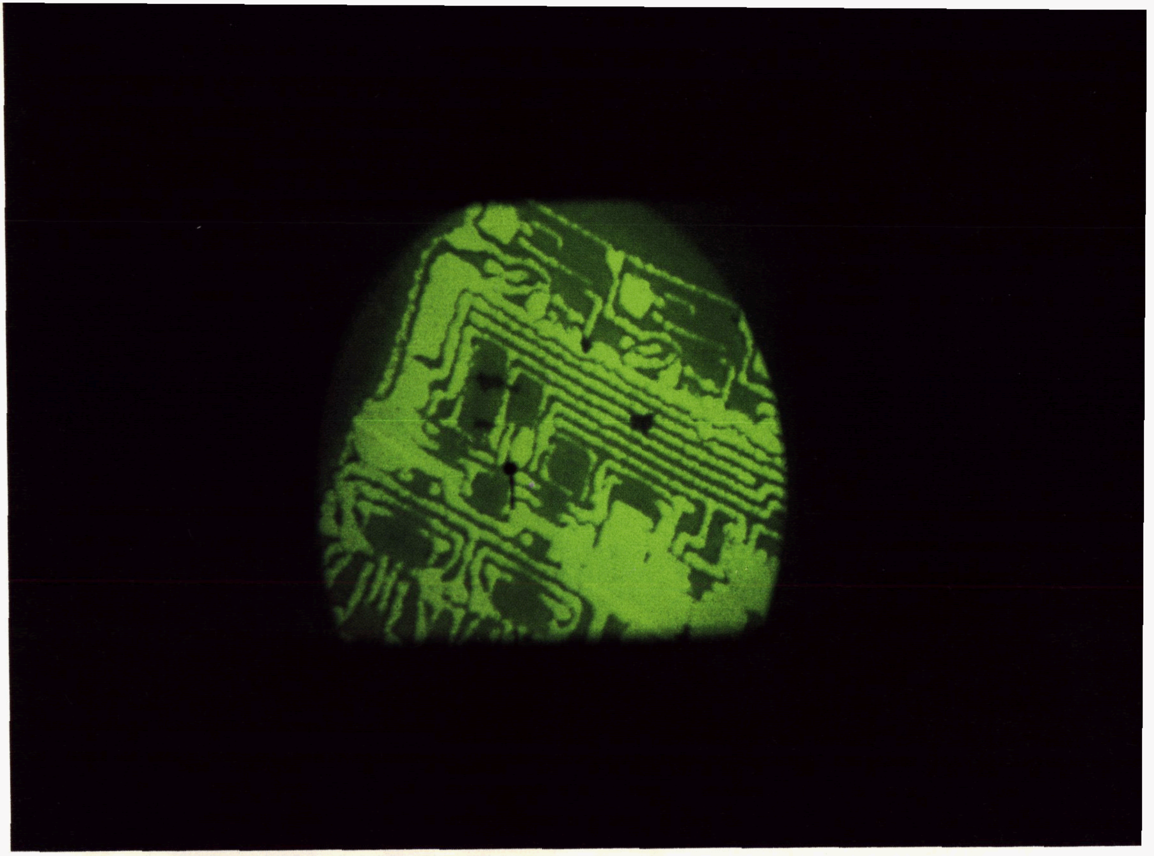
Also needed in this preparation system was a way to hold the specimens after they were sliced. For this, we devised a protective chamber in which the specimens are carefully sealed between layers of ultrathin graphite film through which electrons can freely pass.

One result of the improvements is the ability to make quantitative predictions about the behavior of biological matter. Physicists can make predictions because they can observe or measure basic components. For example, knowing the length of a pipe in a pipe organ and the speed of sound in air, we can predict all the tones and overtones that can be produced. In biology, however, the basic components are molecules, which we have not been able to see. Thus, we have had to work with unpredictable groups of molecules.

The ability to predict in the biological world will have important consequences. Until recently, for example, we knew relatively little about the nature of deoxyribonucleic acid (DNA)—the substance that contains all the data needed to program the construction of a man from his brain to his toenails. Although it is one of the largest molecules, DNA still is extremely small. A human being contains approximately 50 trillion cells, each of which contain 46 chromosomes. These chromosomes, in turn, have more than 1,000 genes, each containing vast numbers of minute DNA ribbons. With the electron microscope we are beginning to be able to view this programming phenomenon, including the transfer of information from DNA to the building centers of the cells by ribonucleic acid (RNA).



Electron microscopes demagnify type, *below*, to a point where letters are only 100 atoms high. Size of page, similar to the one you are reading, is shown relative to specimen grid, *above*. When reduced to the actual size, it is an almost invisible dot.

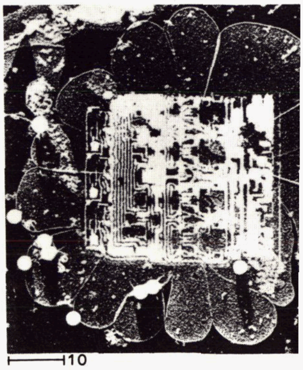


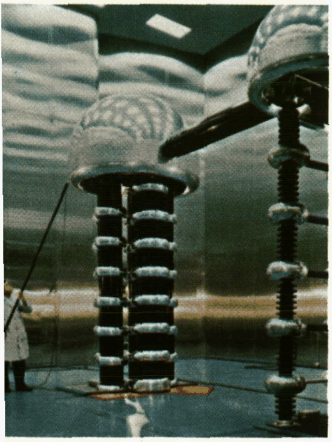
Our primary goal, however, is to view the structure of molecules directly. This means entering the domain of 1 to 2 A. In some materials we can already see the atoms in the crystalline lattice arranged to make up the incredibly complex organic molecules. We have also been able to observe cell membranes. For example, in the subunit structure of myelin–a substance that forms part of the nerve fiber–we have actually watched cells in the process of rearranging their molecular structure.

Because the diamond knife can cut specimens as thin as 50 A, we can now do chemistry by cutting. We can cut up a starch molecule in such a way that it becomes sugar. We can slice a virus in half. It may even be possible to correct genetic errors. For example, we can examine the DNA ribbon in the gene causing hemophilia. It may be possible to edit this ribbon–actually cut into the nucleotides and rearrange them in proper order. The edited DNA could then be copied in great numbers and inserted in a female ovum to crowd out the faulty genes. Since the genetic likelihood of a disease such as hemophilia is relatively easy to predict, this technique could, in a few generations, eliminate the disease.

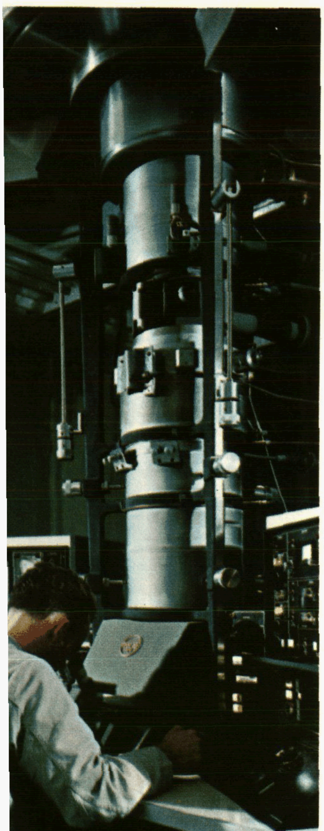
The use of the electron microscope in reverse–to demagnify–also offers many fascinating possibilities. One is the storage and retrieval of information. Using grainless film developed in our laboratory, we can photographically reduce pages, such as the one you are reading, to an almost invisible dot. Letters on such a page are only about 100 atoms

Demagnifying techniques also permit printing electronic circuits, seen in electron microscope viewing port, *above,* onto blood cells or retinal rods, *below.* These circuits can be implanted in the body. The circuit is only about 6 microns across.





Accelerators, *above,* generate electrons for a million-volt RCA electron microscope, *below*. These electrons travel at about 94 per cent the speed of light, with wave lengths to .009 A. High energy electrons can easily penetrate thicker specimens, and provide improved resolution.



high. With the electron microscope, the entire collection of the Library of Congress could be reduced to a single sheet, 8 inches by 10 inches, transferred to micro-tape, and later displayed, page by page, on a television screen.

Further development of the electron microscope's potential in this direction could lead to its use in miniaturized computers. By printing electronic circuits on film and reducing them in the same way pages of type are reduced, we could provide more compact, and thus more efficient, computers. The microscope may also teach us how to duplicate our own ultraminiaturized molecular information storage system—the memory portion of the human brain. The packing density of our brain—the number of working elements in a given volume—is 10 to 100 billion elements per cubic inch. Packing densities of present computer components range up to 1 million elements per cubic inch. By improving this density with electron microscope techniques we would, among other things, greatly enhance the speed of retrieving information.

Holography with the electron microscope may also help explain the memory apparatus of the human brain. Our ability to summon words, sentences, and other behavioral sequences from our experiences seems to be a random and nonlocalized process. We believe that human memory banks are highly repetitive—all the data being stored in every portion of the brain.

The retrieving mechanism may act somewhat like a reverse of holography in which the illuminating laser beam is matched to a hologram to produce the reference beam. One application for visible light holography envisions rapidly passing an enormous file of fingerprints, stored on microfilm, past an illuminating beam that is shining through a hologram of the fingerprint being sought. When the hologram matches the print on file, the reference beam flashes. If we could demonstrate that the brain uses a similar system to summon our thoughts, we would begin to understand the phenomena of perception. Also, we could experiment with the cells or cell clusters responsible for storing sensory information.

A fascinating application for ultrareduced printed circuits could be as a prosthetic sensor. Placed on a red blood cell, it could then transmit information from within the human body. We have already successfully placed an amplifier circuit on a retinal rod—that portion of the eye that reacts to faint light. Such devices, only 6 microns across, could be produced in large quantities and incorporated at key sites of the body where, for example, they could monitor the operation of the nervous system. They would, of course, have to have biosynthetically produced protein coats so they would not be rejected by the immune responses of the body. Using the natural electricity in the body for power, these sensors would transmit neurological electric impulses similar to those recorded by an electroencephalogram. But they would be transmitted by radio, eliminating the need for physical attachments to the body, and permitting the patient to be monitored as he goes about his affairs.

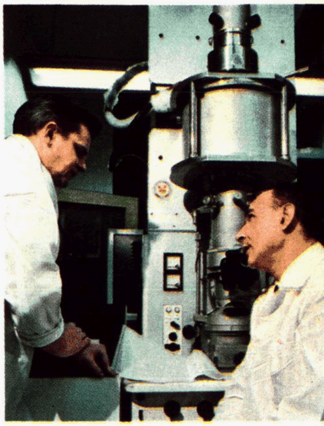
The electron microscope even has a potential for gaining information about the structure and organization of space which, like life itself, is written in the atoms. Atoms throughout the universe obey the same laws, and interstellar dust is only a few hundred atoms in diameter. Thus, much of what we will someday find in space will make sense only if we can examine it at the submicroscopic level. The electron microscope may become the primary tool with which we will define matter far beyond our present concept.

Beginning with Max Knoll and Ernest Ruska in Germany during the 1930s, the development of the electron microscope has been an international achievement. Major advances were made by Francis O. Schmidt and Cecil Hall at Massachusetts Institute of Technology and a Rockefeller University group under the direction of Keith Porter and George Palade. High-voltage instruments were pioneered in France and Japan, and Gabor's work in England, of course, resulted in holography. In our University of Chicago laboratory, we have scientists and technicians from throughout the world, including Cuba, Italy, Japan, South America, and Sweden. I feel strongly that these observatories should continue to have an international character. When a science acquires the unique capabilities we are approaching with the electron microscope, it should not be held the property of one or a group of nations.

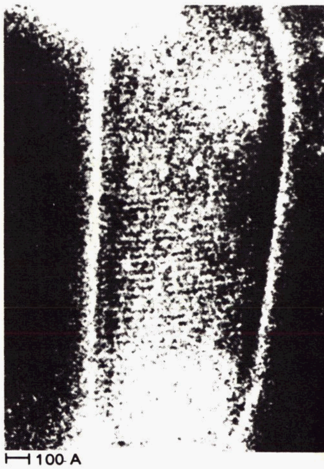
The members of our laboratory also range widely in disciplines, covering both the physical and biological sciences. Our ability to see things that no one has seen before and to think about them in a way no one has thought about them, will depend on extending this range of disciplines. We will need scientists familiar with crystallography, modern mathematics, and quantum mechanics.

The greatest need will be for highly skilled operators. Operating a microscope is much like playing a fine musical instrument. The quality of the performance, requiring intuitive and interpretive abilities, depends on the talent of the performer. He must have a good ear, a good eye, a good hand–and patience.

This marvelous instrument has begun to show us how intimately man is linked to the domain of atoms and how minute matter in the universe influences his destiny. New concepts in this technology will someday permit us not only to predict, but also to design life at the molecular level. Scientists will have a power more awesome than any ever imagined. In turn, they will have the grave responsibility of using this power wisely.



The author created and developed the ultralow temperature electron microscope. Promised improvement can be seen in the photomicrograph, *below*, which shows the lattice structure of the enzyme, catalase.



For further reading:

Bradbury, S., *The Evolution of the Microscope,* Pergamon Press, 1967.
Cosslett, V. E., *Modern Microscopy,* Cornell University Press, 1966.
Freundlich, Martin F., "Origin of the Electron Microscope," *Science,* Vol. 142, Oct. 11, 1963.
"One-Atom Microscope," *Scientific American* (Science and the Citizen), March, 1968.

A Science Year Report

By Robert S. Hoffmann

Russian Science: A Personal View

Printed in U.S.A.

E-165

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FIELD ENTERPRISES EDUCATIONAL CORPORATION

MERCHANDISE MART PLAZA • CHICAGO 54

I.R-100 AWARDS BANQUET
LECTURE

HUMANITY AND SCIENCE AT THE CROSSROADS

Dr. Humberto Fernandez-Moran
Professor of Biophysics
University of Chicago

October 4, 1968
New York Hilton

WELCOME to a unique exhibit and banquet—the annual **I·R 100!**

Here the best of the nation's innovators, those who have distinguished themselves by developing the 100 most significant new technical products of the year, are honored and their new products exhibited.

The **I·R 100** Awards, considered by many as the applied research equivalent of the Nobel Prize, are presented by Industrial Research Inc. to stimulate and recognize the scientific and technological achievements of the nation's $25.5-billion research industry. Since the **I·R 100** began in 1963, some 300 industrial, university, and government laboratories and more than 1,000 scientists and engineers have been cited.

These innovators of modern technology truly represent the best technical minds in the country today.

Their 100 products are selected (from about 10,000 new technical products developed each year) by the Editorial Advisory Board of Industrial Research Inc. This 30-man panel includes five Nobel laureates, heads of research institutes and laboratories, and the inventors or discoverers of radar, stroboscopic photography, radiocarbon dating, galactic astronomy, communications satellites, the laser, and many other scientific accomplishments of our time. (See inside back cover for a listing of the judges.)

A few facts about the 1968 winning products: This year's awards took an average of 29 months to develop—two months more than the average for last year's I·R 100 winners. The cost of developing a winning product was $422,000, on the average, compared with $250,000 last year. Only 17 of the products were developed with the aid of federal funds, compared with 26 a year ago. It would take $1.3-million to purchase all of the 100 winning products this year—or about $22,000 per product.

The entire **I·R 100** exhibit and formal banquet are part of National Industrial Research Week (Sept. 29 through Oct. 5) being observed by the nation's 15,000 industrial laboratories. Open houses, exhibits, and other activities have been scheduled during this Week to call attention to the contributions of the 350,000 scientists and engineers in this country engaged in applied research and development.

Among activities during the Week are an open house at Outboard Marine Corp.'s laboratory in Milwaukee, exhibits at Varian Associates in Palo Alto, a science career program by Xerox in Rochester, and a community salute to U.S. Steel Corp. and other companies with research facilities in Monroeville, Pa.

General Electric, Ford, Sperry Rand, Univac, Westinghouse, Thiokol Chemical, and many other companies also are scheduling special events during National Industrial Research Week.

The National Conference on Industrial Research is held during this Week too. Limited to about 500 corporate presidents, research directors, and senior scientists and engineers, the conference is concerned with making new product development more effective and profitable.

During the research conference two annual awards will be made. The "I·R Man of the Year" award and $1,000 check will go to Dr. Bernd T. Matthias, professor of physics, University of California at San Diego, and technical staff member of Bell Telephone Laboratories, for his achievements in increasing transition temperatures of superconductive materials. And the "I·R Laboratory of the Year" awards will be made to several new outstanding research laboratories.

All of these events, awards, and activities are sponsored by Industrial Research Inc., publishers of *Industrial Research*, *Materials Applications*, *Oceanology International*, and *Electro-Technology* magazines. Purpose of the **I·R 100** and associated events is to stimulate our country's vital "industry of innovation" and to honor outstanding applied research achievement.

Neil P. Ruzic
president
Industrial Research Inc.

THE I•R 100 COMPETITION AND NATIONAL CONFERENCE ON INDUSTRIAL RESEARCH

The *I•R 100* Competition and the National Conference on Industrial Research are sponsored annually by Industrial Research Inc. as a service to the nation's $25-billion research industry.

The 100 most significant new technical products of the year are selected in the *I•R 100* Competition. The products are displayed and their developers honored at the annual product exhibit and awards banquet.

The conference, which has "New Products — and Profits" as its theme this year, is sponsored by Industrial Research Inc. in cooperation with the Purdue University Krannert Graduate School of Industrial Administration, IIT Research Institute, and Battelle Memorial Institute.

I•R 100 SPECIAL SECTIONS

A complete report on the *I•R 100* winning products will be featured in the December issue of *Industrial Research.* Descriptions of the prize-winning electronic products will be published in the December issue of *Electro-Technology,* while a summary of oceanographic product results will appear in the December issue of *Oceanology International.*

Schedule of Events

NATIONAL CONFERENCE ON INDUSTRIAL RESEARCH
and I•R 100 Awards Program

Oct. 3-4, 1968

THURSDAY, OCTOBER 3

8 to 9 a.m.	Conference registration	Ballroom Foyer
9 to 12 p.m.	Conference morning session	Trianon Ballroom
11 a.m. to 7 p.m.	"I•R 100" exhibit	Rhinelander Gallery
12:15 to 2 p.m.	Conference luncheon	Mercury Ballroom
2 to 5 p.m.	Conference afternoon session	Trianon Ballroom
Tour of	"I•R 100" exhibit	Rhinelander Gallery

FRIDAY, OCTOBER 4

9 to 12 p.m.	Conference morning session	Trianon Ballroom
11 a.m. to 7 p.m.	"I•R 100" exhibit	Rhinelander Gallery
12:15 to 2 p.m.	Conference luncheon "I•R Man of the Year" award presentation	Mercury Ballroom
2 to 5 p.m.	Conference afternoon session	Trianon Ballroom
6 to 7 p.m.	Reception	Rhinelander Gallery
7 to 9:30 p.m.	Industrial Research awards banquet	Grand Ballroom
	"I•R Laboratory of the Year" and "I•R 100" awards presentation	

KEYNOTE SPEAKER at the **I•R 100** formal banquet Friday night, Oct. 4 is Dr. Humberto Fernandez-Moran, often called a "renaissance man." Biophysicist, physician, neurologist, neuropathologist, radiation authority, inventor of cryogenic electron microscopes, philosopher, and former diplomat for Venezuela, Dr. Fernandez-Moran will address the innovators of the nation's most significant new technical products on "Humanity and Science at the Crossroads."

I.R-100 LECTURE (Oct. 4, 1968)

H. Fernandez-Moran

INTRODUCTION

On rare occasions such as these, we are privileged to share and live through the high noon of an era which is rapidly moving towards a critical point of transition in space and time. Its thundering "leitmotiv" started reverberating about a quarter of a century ago with the controlled release of nuclear energy brought about through the concerted efforts of a group of dedicated men, many of whom are still among us, like Dr. Glenn Seaborg who addressed you last year, and Dr. Alexander Sachs, one of its inspired originators, who is here tonight. Since then, accelerated scientific and technological progress in all fields has enabled Man to visualize directly the complex structure of atoms and molecules in living matter, to venture out into space, and in general to achieve remarkable feats in control and communication on a planetary scale, vastly extending his intellectual powers--until now we confront a strange future laden with deep uncertainties and grave challenges, but still offering ever greater opportunities.

Resurrecting the conceptions of one of the boldest thinkers of all time, who worked and died in this city barely 13 years ago: Pierre Teilhard de Chardin, we must admit that Mankind has now reached a crucial stage, Mankind is perplexed and even bored, not knowing what to do with itself and yet paradoxically endowed with unprecedented potential for good or evil. It may not be the shallow "brave new world" once predicted, but it certainly is one of the most active and demanding, more attuned to the faith and vision of the optimist, than to the paralyzing confusion of the pessimist.

We are all keenly aware of the social turmoil affecting particularly the younger generation at the national and international levels; and the terrible "memento mori" has not ceased to haunt our era since 1938, dimming the full joy of a Promethean renaissance. In addition, the 'population explosion' is already so overwhelming that by the 1970's hundreds of millions of people are going to starve to death in spite of any foreseeable emergency programs which can now be implemented.

Yet, it is against this background of stark realism that I wish to invoke the spirit of individual innovation representative of this forum to state the central thesis that cooperative endeavors of human minds guided by science and technology will ultimately lead Mankind to higher levels of inventiveness and achievement.

This stems from our 'faith in Man' and his future which gives us the conviction that just as we appear to have reached the "critical mass for annihilation" under unrelenting biological and social pressures, so have we been likewise invested with an ample 'critical mass' capacity for survival and further evolution. As expressed by Faulkner in his memorable Nobel Prize speech: 'Man shall not merely endure, he shall prevail on this Earth', and all that Mankind stands for is inextricably linked to the progress of the Universe.

Man, the Thinker, the Believer, and the Dreamer, is at the very heart of the Cosmos. In this deeper sense, Man himself is the missing link.

Moreover, Man is a Trustee of Life, one of its many forms in the Universe. Therefore, he must fulfill the dual obligation of ensuring his own survival, while trying to preserve and understand all other forms of Life, no matter how alien. I understand Albert Schweitzer's 'Reverence for Life' primarily in this sense.

Perhaps the only permissible constraint that Man can invoke and exercise may be derived from an analogy to Pauli's exclusion principle. Since according to this principle (which I termed 'Vivethics'), no two forms of Life can 'occupy' or 'inhabit' the same time-space domain, Man could ultimately justify pre-empting other forms of Life inimical to his own existence, but he may never wantonly destroy or kill them. In general, from a 'rational point of view', the ethical principles may be literally a fundamental condition for survival and higher evolution of the human race.

So many great minds and hearts have already wrestled with these problems and pointed out possible solutions, that I can only aspire here to deal with certain salient approaches in the need for developing more effective methodological and conceptual tools for probing the future. I should like to set forth some of these more as a list of seminal problems which can be posed from a biophysicist's point of view to stimulate the interest and active participation of scientists and technologists focusing on key areas of the Neurosciences in exploring the human mind, of Molecular Biology, of Exobiology, and of Biomolecular Organization at all levels.

There is one specific 'case history' which I wish to dwell on--not only because it is eminently timely in light of recent events, but also because of its decisive historical and geopolitical significance.

Its urgency becomes manifest as we realize the serious threat to the whole future of our species inexorably building up when more than half of the world is hungry, many are starving to death, and we still keep on growing at such a rate that the present population of well over three billion people is expected to double within the next 30 years on a sick planet already in the grip of environmental deterioration, pollution and declining natural resources. To counteract a vicious circle of such planetary proportions, the world population must rapidly be brought under control, through voluntary, conscious regulation of human reproduction coupled with an integrated program designed to increase food production greatly and achieve environmental restoration. This could mean such an abrupt reversal of a previously uncontrolled evolutionary trend that we would have to postulate the action of highly cooperative phenomena embracing basic affinities of the individual human minds, not unlike those involved with manifestation of quantum effects operating on a truly macroscopic scale, of which superconductivity is a remarkable example.

In any case, it is interesting to consider such cooperativity phenomena effective within certain collective domains on a social-geopolitical scale as being first localized and 'regional'. Ultimately, however, these 'Homo-cooperativity' processes could extend over the entire system and achieve international siginficance through purposeful, systematic interaction with technological communication media.

I submit that nowhere on this planet are conditions more favorable for attainment of true cooperativity phenomena at the present time than between the Americas. To begin with, the United States may be regarded as the typical and most successful example of such Homo-cooperativity phenomena. Thus, when Henry James defined Americans as "people of abysmal good nature and ultimate good sense," as Dr. Alexander Sachs recently told me, he was expressing the qualities which are essential for true cooperativity among human beings. Precisely this rare quality of being able to elicit the best efforts from individuals of all nationalities without distorting them in the process, accounts for the phenomenal success of the American 'team effort' ranging from the economic to scientific and engineering cooperative projects. It explains why the U.S. now controls two-thirds of the world's capital market, using only about five per cent of the world's highly qualified labor force to do so. It also helps explain why the U.S.A., representing less than 1/15 of the world's population uses over half of all the raw material consumed each year.

In fact, this inherent capability for success has "activated" this enterprising nation to such a degree that it has unfortunately disposed or squandered its own resources with such prodigality, and it now finds itself lacking basic raw materials, and entangled in so many global commitments by virtue of its dual role of World banker and World philanthropist, that it is facing a generally estranged or hostile world.

And that in itself is a fundamental reason for turning to its other neighbor nations in Canada and Latin America at this crucial point of history.

Basic supporting factors for these cooperative projects between the Americas are the geopolitical proximity and the complementarity in filling each other's needs. U.S. primarily needs natural resources and markets; while Latin America essentially needs assistance in filling the technical, scientific, and managerial gap. Both inseparable halves of the great Continent most definitely require to know each other b[illegible]r, both as individuals and as social entities, as well [illegible] actively exchange the wealth of their cultural heritage at all levels.

Latin America as a whole now emerges as the only "viable" continent invested with the greatest untapped stores of prime resources. The entire continental United States can, for example, be emplaced in the gigantic Amazon valley, which contains, among many other things, 25% of the world's timber, its greatest river and drainage system, etc. Despite manifest social ailments, Latin America turns out to have a remarkable bedrock strength in its closely related common languages, religion, unusually complex but vigorous genetic background. Blessed with great biological survival features, it enters the historical scene precisely at the time that our advanced technology (including nuclear engineering) permits us to cope effectively with the formidable barriers, now become instead welcome challenges and opportunities.

This would range from nuclear explosion and earth-displacement programs to form dikes and hydro-electric transportation networks interconnecting the Amazon, Orinoco, and Paraguay systems, to the use of integrated atomic power-reactors and petrochemical complexes, with "synergistic" minerals, agricultural, hydroponic, timber, and related development projects. Much of this has already been adumbrated by an increasing number of U.S., Latin American and European planners, including most recently the imaginative group of Panero and Kahn at the Hudson Institute (article in Fortune, December 1967, p. 148).

In order to be really successful on a long-term basis, these cooperative projects between the U.S.-Canada-Latin America should comprise a fully integrated program to fill the gaps primarily at the functional levels: general economic gap, foreign investment gap, research and development gap, a management gap and an education gap.

The educational gap is at the heart of the problem, encompassing secondary, technical and graduate schools, and particularly the modern American management education (e.g. Harvard's Business Management Institute), and the new technical graduate schools patterned after those two centers of excellence: M.I.T. and CalTech.

There will likewise be a great need for several "multiversity"-type international universities for key regions of Latin America. As we envision it, they would be an internationally-financed community with an international faculty, representing the professional excellence of a number of countries. They would have international classrooms connected by transcontinental electronic communications systems; international laboratories in which a U.S. and a Latin American student--each on his own campus--could cooperate on a scientific experiment; and international repositories of information coupled with computer retrieval facilities (Scientific Research, S. Winer, January 1968).

It is my firm conviction that America is an indivisible entity, which will either survive and fulfill its historical destiny as the backbone of this planet in a complete and voluntary cooperation between North and South, or disintegrate piecemeal. This complementarity is not hypothetical, but rests on solid historical background. Remember that Bolivar already conceived and laid the foundation for a "Pan American Union" nearly a century and a half ago. Following Bolivar's death, certain circumstances, notably the massive immigration from Europe in the 1840-50's, definitely favored the North; and it has since retained a historical preponderance while South America recovered from its hemorrhages and wrestled weakly as a sick giant with the titanic handicaps of its tropical domain. Now, the pendulum is gradually swinging the other way, and it takes intuition of rare order and great thoughtfulness and understanding to bring about a true cooperative "resonance" between the twin continents.

In closing, let me thank you for your hospitality and understanding. I can find no better way to convey the feeling of silent hope and reverence that we all cherish when we think of our common heritage and future destiny than to quote those immortal words of Simon Bolivar, one of Mankind's greatest statesmen and seers, from his Address delivered at the inauguration of the Second National Congress of Venezuela in Angostura, February 15, 1819:

> "My imagination, taking flight to the ages to come, is captured by the vision of future centuries, and when, from that vantage point, I observe with admiration and amazement the prosperity, the splendor, the fullness of life which will then flourish in this vast region, I am overwhelmed. I seem to see my country at the very heart of the universe.....I behold her shipping to all corners of the earth the treasures.....which lie hidden in her mountains. I can see her dispensing....health and life to the ailing....I can see her confiding her precious secrets to the learned men who do not know that her store of knowledge is superior to the wealth with which Nature has prodigally endowed her."