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SCIENTIFIC INNOVATION AND RESONANCE IONIZATION SPECTROSCOPY*

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Good morning, ladies and gentlemen. It is my pleasure to welcome you to the Symposium on Resonance Ionization Spectroscopy and Its Applications. I would like to speak to you this morning on the important topic of scientific and technical innovation — more specifically, how do we as scientists, engineers, or science administrators encourage the transfer of technology to the market place? Although it may seem to some of you to be a non-problem, I can assure you from personal experience that this is not so. I hope that I can give you several examples from my own experience on this important issue of transferring the fruits and labors of scientific investigation to private industry.

I will try to avoid the use of terms such as "basic" or "applied research." It has been my experience that, very often, the use of such terminology or substitutes such as "fundamental" and "mission-oriented reseach" have only led to unnecessary confusion and obfuscation. To emphasize my point, I would like to share with you an illustration (Figure 1) from M. C. Escher to which I have added my own interpretation of fundamental and mission-oriented research (I promised not to use the words "basic" and "applied"). In my view, the space in which research is done can be likened to a Mobius strip, which as you know, has one continuous surface. Fundamental and mission-oriented research often lie on the same path, and what might appear to be fundamental research at one point in time might prove to be very mission-oriented at some later point in time. Please note also that problems can enter the strip from any direction or spin off in any direction. Thus some research which appears at first to be mission-oriented can often result in research questions of a very fundamental nature. Obviously, the reverse is true. My talk will dwell primarily on the latter situation in which we are trying to spin off mission-oriented or practical applications from fundamental discoveries.

In 1396 Henri Becquerel accidentally placed some uranium salts on covered photographic plates in a darkened drawer. The German scientist, Martin Heinrich Kloproth, had isolated the uranium salts from pitch blende ores some 107 years earlier. Becquerel developed the photographic plates and recognized that the uranium salts were the reason the plates had been exposed. For this Becquerel and the Curies shared a Nobel Prize. The rest is history — Hahn and Strassmann, Stagg Field, Alamogordo, nuclear powered submarines, satellites powered by nuclear batteries, and commercial nuclear power reactors.

Shortly after Becquerel's discovery of radioactivity, Roentgen used film to make radiograms and, in time, many kinds of radiation detectors were developed. Scientists learned that radiation passing through certain materials such as zinc sulfide produced flashes of light that could be seen without the aid of instruments. Lord Rutherford and his students sat in a darkened room observing flashes of light from alpha rays with a spinthariscope. The spinthariscope was simply a zinc sulfide coated optical eyepiece. Thus, one atom detection (OAD) or, more correctly, helium nuclei, in one sense is not a recent phenomenon. I can also recall sitting in a darkened room at the Los Alamos Scientific Laboratory with Drs. Ernest Anderson ar Newton Hayes in the late 1950s looking for scintillations signallir the interaction of radiation with various liquid scintillators under development at the Laboratory. The Los Alamos group learned how to place an experimental animal or person in an annular space surrounded by a large tank of liquid scintillator solution in virtually a four-pi steradian counting geometry (Figure 2). Scintillations detected within the tank were recorded, amplified, and crudely sorted by energy, as shown in Figure 2 which schematically represents a liquid scintillation gamma-ray detector used for rodents.

Figure 3 shows an early version of the Los Alamos Small Animal Counter comprised of the detector and its associated electronics. In 1958 at the first meeting of the newly created Health Physics Society, we described such a system for measuring gamma emitting radionuclides in experimental animals (1).

Energy resolution was good enough to allow the detection and quantitation of fallout ^{137}Cs and naturally occurring ^{40}K gamma rays from living subjects or experimental animals. Figure 4 shows a schematic of the Los Alamos Human Counter II (HUMCO-II). An earlier version used a cylindrical shield, rather than a steel room, around the detector. The increasing use of radioactive materials by industry, research, and medicine in the 1950s helped promote the construction of detectors capable of measuring small amounts of radioactivity in patients or accidentally exposed individuals. Because the measurements were non-destructive, the sample could be measured repeatedly over time. Whole body retention kinetics were established for numerous gamma-emitting radionuclides in several mammalian species.

Members of the Los Alamos team left the Laboratory to join private companies, and assisted in making whole-body liquid scintillation detectors for in vivo measurement of gamma-emitting radionuclides commercially available. In a similar fashion, the technology related to solid state detectors, which possess much better spectral resolution, was transferred from the Atomic Energy Commission's laboratories to private companies. As you know, this process of measuring parts or all of the human body following the administration of radionuclides has led to the commercial development of very sophisticated instrumentation.

By 1964 human counters using organic scintillators were distributed worldwide, including the United States, Canada, England, Germany, and Japan. A large number of companies produced and sold organic scintillators for small animal, arm, and human counters. More detailed information on the companies involved in producing counters or scintillators was reported in 1967 (2).

This successful technology transfer story reminds me of the statement made by Dr. Chien Shiung Wu, Pupin Professor of Physics, Columbia University (Figure 5). Dr. Wu said,

> "Basic science has often been described as the fountainhead of new knowledge. It must be kept continuously flowing. Then applied research may be looked upon as streams and brooks which lead the spring to our fields and meadows where it can best serve the human needs."

For many years I worked with Dr. Wright Langham at Los Alamos. We often discussed the problems encountered in getting scientists to "turn loose" of instruments and discoveries. It seemed as though things were never quite right or ready, HUMCO I became HUMCO II, and model 4 became model 5 and so on. We would even have problems with physicists and instrumentation engineers not wanting to release new equipment to their biological colleagues down the hall. Often the argument was that "the next version will be much better," or "let me make one or two modifications." Wright and I called this the "weaning problem."

I recall the development of the cell separator and sorter at Los Alamos. This invention used a laser beam to interrogate chemically stained biological cells as they passed in single file, while contained in small fluid droplets, past the beam. I thought this example of innovation might also be appropriate to our discussion because it involves lasers as does the resonance ionization spectroscopy phenomenon. A Swedish scientist named Lagerquist was the first to count erythrocytes (red blood cells) by photoelectric methods. Others in England developed a liquid-sheath flow system with entrainment and photoelectric detection into an improved erythrocyte counter. Finally, electrical-resistance counting, known as "Coulter counting," was invented by Wallace Coulter in the mid-1950s. Coulter's system for erythrocyte counting and volume spectrometry was built upon by scientists and engineers in the United States and other countries. This led to the investigation of optical scattering, absorption and fluorescence measurements of both stained and unstained biological cells. These activities culminated in the development of flow microfluorometry systems by the Los Alamos group, several other laboratories in the United States, and groups in Freiburg and Munster in Germany. These groups concentrated primarily on the use of cells stained with fluorescent dyes. In addition, several groups at the Los Alamos Scientific Laboratory and in private companies concentrated more on light scattering and absorption phenomenon. Fulwyler at Los Alamos invented electronic cell sorting based upon the Coulter principle. Figure 6 shows schematically the major components of a multi-parameter cell separator. These include the flow chamber, laser beam, generation of droplets, droplet charging, and a deflection scheme which allow sample collection of the deflected droplets.

Dr. M. A. Van Dilla gives a more comprehensive history of these developments in the Proceedings of the First Los Alamos Life Sciences Symposium held in 1973 at the Los Alamos Scientific Laboratory (3). That symposium, entitled "Mammalian Cells — Probes and Problems," was held for several reasons, one of which was to expedite the application of flow systems to biomedical research. Perhaps the major factor involved in the transfer of much of the technology developed at the Los Alamos Scientific Laboratory in the area of flow cytometry occurred when Dr. Mack Fulwyler left the Laboratory to become associated with Coulter Electronics in a laboratory established at Los Alamos. Other researchers associated with the development of flow microfluorometry also became associated with private industry. At first this type instrumentation was regarded primarily as a research tool, which means that it was relatively expensive with a resultant small market and high risk for the developers. This situation has changed with time, and cell sorters and separators are now becoming more commonplace in the biomedical and biological research laboratories.

RIS was raising hopes and was a cause for celebration when I came to Oak Ridge National Laboratory in 1974. I recall the excitement as Sam Hurst and his colleagues demonstrated proof of principle for the use of RIS for single atom detection. I also remember referring to one-atom detection in the Failla memorial lecture (4) which I presented to the Radiation Research Society in 1976 in San Francisco. In the section of my lecture entitled "How Well Can We Detect Environmental Pollutants?" I referred to the book by Lowrance (5) entitled "Acceptable Risk," which stated that, paradoxically, most public controversies arise because our ability to assay physical phenomenon has become extraordinarily sensitive. We hear this argument expressed quite often in the context of RIS and OAD when people say, "Now that we can detect a small number or, in fact, one atom, the regulatory standards ultimately will reflect that change." Lowrance argued that in many cases we can only measure signals above the noise level and perceive things that were previously blurred or not at all detectable. He also argued that we may find ourselves holding a lode of data whose significance we cannot yet understand. In the Failla lecture I stated the following:

"Lowrance reminds us that the controversy over DDT arose in part simply because we learned how to detect a chemical with great sensitivity. The almost ubiquitous distribution of DDT in living organisms, including human beings, around the world was hard evidence that could not be ignored, no matter how small the level of contamination.

"The severity of water-borne diseases and disease epidemics has been significantly reduced because of the use of disinfection treatment of sewage and potable water. In the past fifty years, the principal disinfectants used have been chlorine and ozone; however, we have only recently understood how chloro-organics are formed during disinfection of sewage effluents and potable water with chlorine. This knowledge is directly attributable to the development of extremely sensitive analytical techniques during the last decade. It makes one speculate as to what will happen in the future when we refine our detection sensitivities to the level of one or perhaps several atoms in a given sample. This may be closer than many realize. For example, at the Oak Ridge National Laboratory, we are now working on one atom detection capability using resonance ionization spectrometric techniques. The research team working under Dr. Hurst at the ORNL has detected as few as ten atoms on one occasion, and has achieved detection of a single Cs atom."

In June 1978 we held a workshop at the Laboratory to encourage private organizations to exploit RIS and OAD applications. A January 1978 workshop was canceled because of lack of interest. I was surprised when both attempts to transfer the technology from the Laboratory to private industry appeared to fail. I have urged Dr. Kaye, Director of the Health and Safety Research Division, to continue to try to interest private enterprise in this technology. I have also asked others why there appears to be little interest on the part of private organizations to develop RIS and OAD techniques. We are aware of some problems involving patents. It seems to me that such a powerful tool would sooner or later be worth the risk of capital investment by private organizations.

One of ORNL's major goals is to perform long-term, high-risk research and to transfer results to the scientific and industrial communities. We seek joint programs with industry via several mechanisms. These include: technology transfer projects where industry is encouraged to utilize our research developments; collaborative research in which industrial personnel work with our staff; user facility programs where industry uses our resource facilities for their own work; and conjoint programs in which a company funds us to perform long-term R&D specifically for them.

There are infrastructural problems which are being negotiated and, as the patent policy and other key issues are clarified, the situation will become more attractive to industry. In the final analysis, everyone should benefit from these activities. The European nations have learned to better utilize their national research facilities for improving their scientific, technological, and, in fact, economic positions in the world community. I think we have some catching up to do in this regard.

This symposium, in part, was developed because of our interests in transferring this important technology to the private sector. We will hear a great deal about the vast capabilities and probably some limitations of this instrumentation. It is my sincerest hope that this meeting will accomplish several goals, one of which is to stimulate an interest in exploiting RIS and OAD as a research tool and another to stimulate interest in transferring the technology from the laboratory to the market place.

In closing, I must share one observation concerning RIS with you. Last fall I participated in the symposium at the Los Alamos Scientific Laboratory. On the program was a paper entitled "History of Radiation and Its Uses" by H. M. Parker (6). Mr. Parker recounted what he views to be the most important and significant developments in the radiation field beginning with Roentgen's publication (7) in 1895 entitled "On a New Kind of Rays." He lists major developments by Becquerel, the Curies, Rutherford, Geiger, Bohr, Bragg, Compton, Cockroft and Walton, Chadwick, Fermi, Hahn and Strassmann, Meitner and Frisch, and ends, I think, appropriately, with the following citation. "The ultimate in sensitivity," G. S. Hurst et al., "Resonance Ionization Spectroscopy and One Atom Detection," Review of Modern Physics 51, 767--819 (1979).

I thank you.

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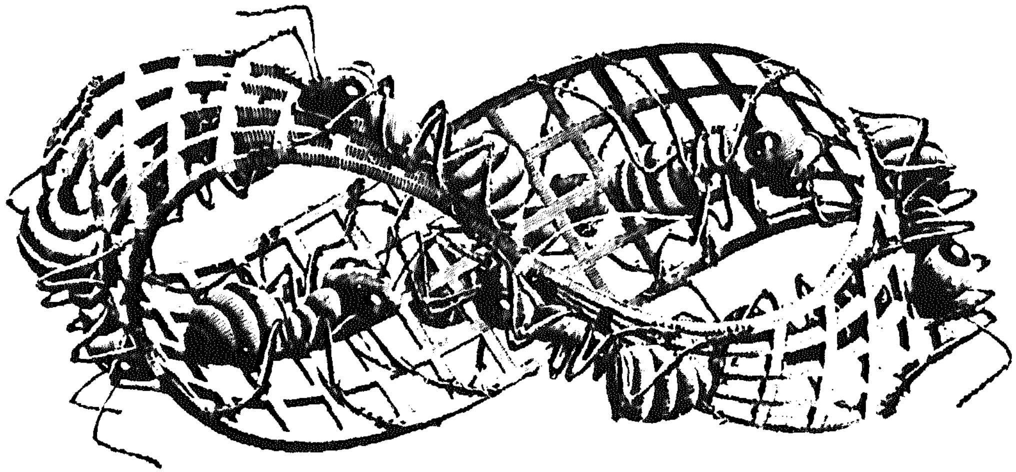

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Figure 1

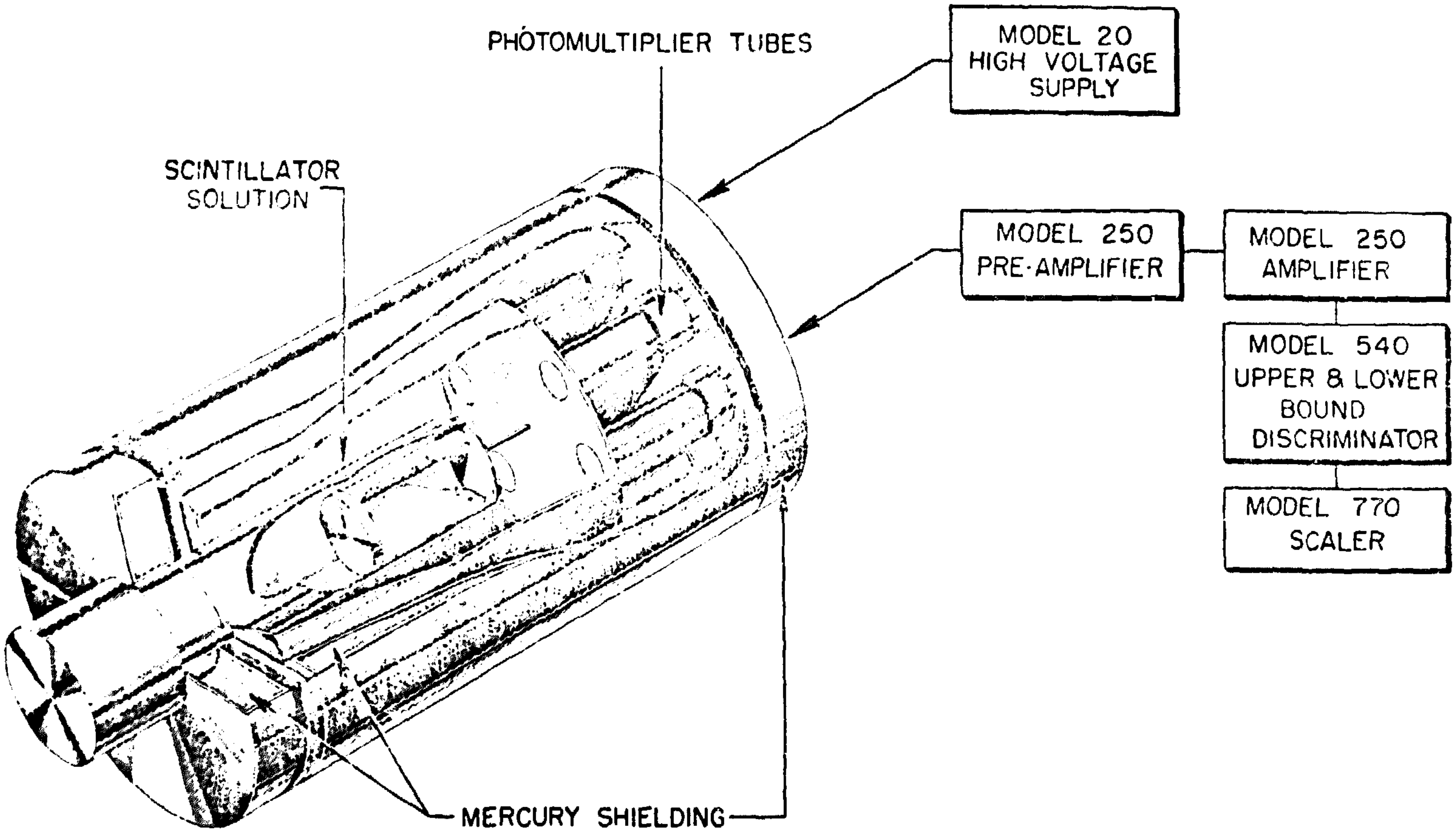
PHOTOMULTIPLIER TUBES
SCINTILLATOR SOLUTION
MERCURY SHIELDING
MODEL 20 HIGH VOLTAGE SUPPLY
MODEL 250 PRE-AMPLIFIER
MODEL 250 AMPLIFIER
MODEL 540 UPPER & LOWER BOUND DISCRIMINATOR
MODEL 770 SCALER

Figure 2

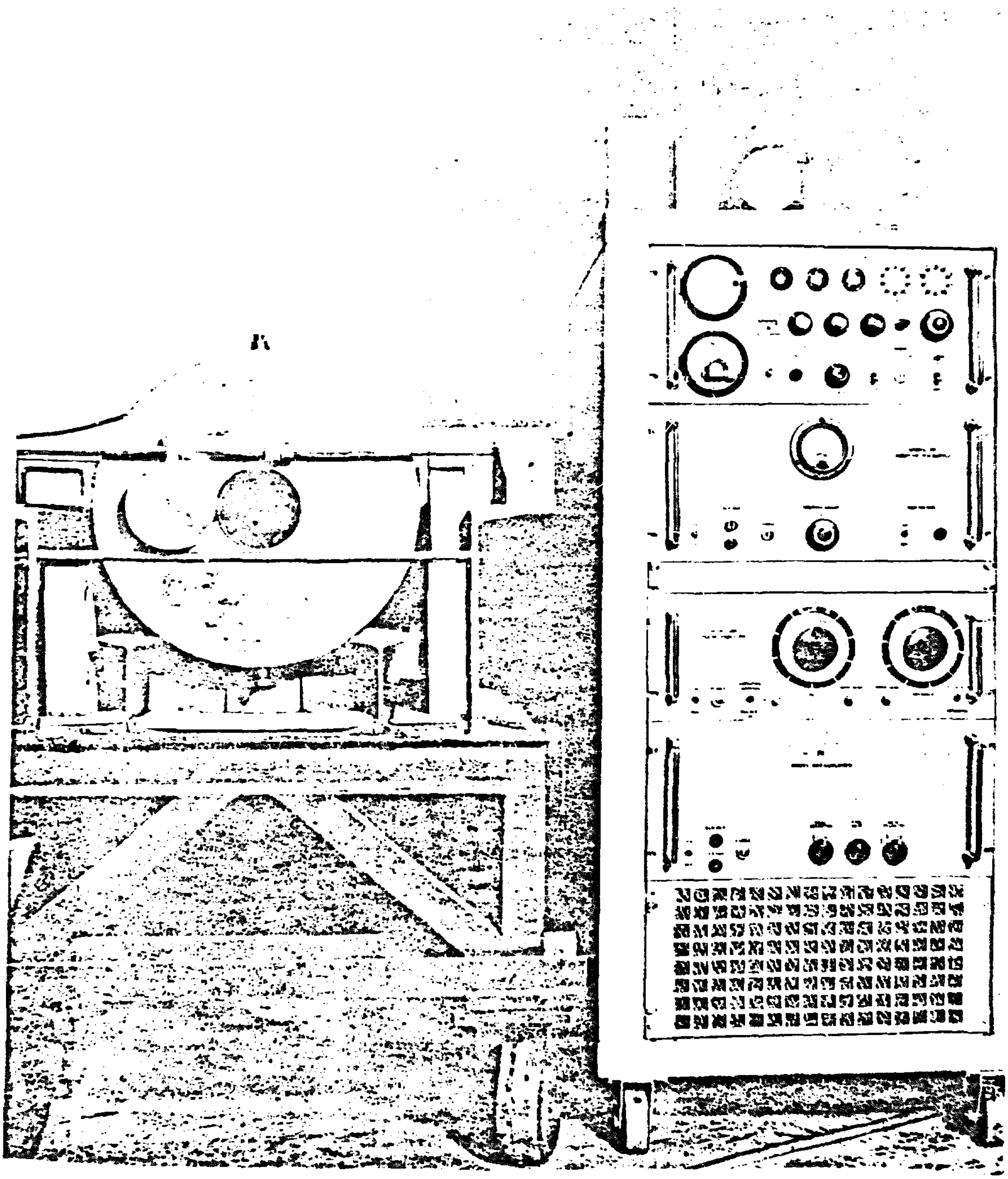

Figure 3

"BASIC SCIENCE HAS OFTEN BEEN DESCRIBED AS THE FOUNTAINHEAD OF NEW KNOWLEDGE, IT MUST BE KEPT CONTINUOUSLY FLOWING. THEN APPLIED RESEARCH MAY BE LOOKED UPON AS STREAMS AND BROOKS WHICH LEAD THE SPRING TO OUR FIELDS AND MEADOWS WHERE IT CAN BEST SERVE THE HUMAN NEEDS."

Dr. CHIEN SHIUNG Wu
PUPIN PROFESSOR OF PHYSICS
COLUMBIA UNIVERSITY

Figure 5

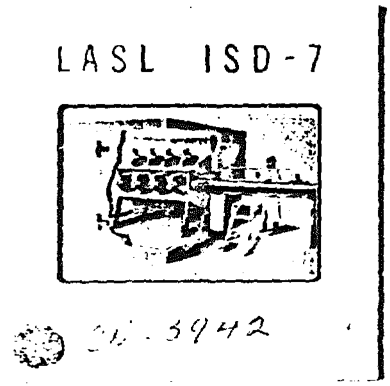

Figure 4

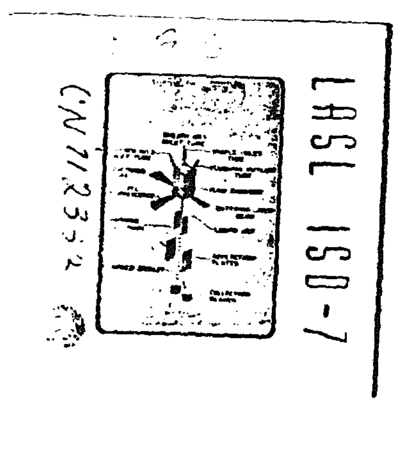

Figure 6