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Accomplishments of The Oak Ridge National Laboratory

Seed Money Program

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Foreword

The Seed Money research program at the Oak Ridge National Laboratory is now entering its twelfth year of accomplishment. Although modest in budget, its focus on new and innovative research appears to have had significant leverage on the changing course of the Laboratory's larger body of work. A review of its history and some of its more tangible results is instructive to all of us concerned with promoting increased public benefit from scientific research.

This report, stemming from an assessment of the Seed Money program performed by my Office of Program Analysis, is a brief and readable account of 12 successful scientific endeavors. While the subject areas of these stories are defined broadly, encompassing in some cases entire fields of research, all share a common link. The Seed Money program provided resources at a crucial juncture in the progress of research. Each accomplishment made a significant or even seminal contribution to the Laboratory's ongoing efforts in each field.

Although numerous program sponsors provided support for much of the underlying foundation of human resources, equipment and facilities, and also provided subsequent resources required to carry these projects to fruition, the Seed Money program provided an important element of creative flexibility. This flexibility both encouraged and enabled researchers to seize opportunities in a timely fashion and pursue them at will across disciplinary, programmatic, and organizational boundaries. The significance of the resulting accomplishments, when set in the proper context as these stories are, may be clearly appreciated by all.

In a larger sense, these stories also offer a unique perspective on the process of basic research and scientific innovation. They show that major advances can be as serendipitous as they are methodological. Successes are frequently born of initial disappointment. Certain investments in research, seemingly well founded and insightful in retrospect, are highly tentative and risky in prospect. With the reading of these stories, one's awareness of uncertainty in research is heightened. So too, however, is one's confidence in the overall process confirmed.

Today, each of the Department's National Laboratories successfully operates a program of exploratory studies, modeled on many of the same principles of R&D management that formed the basis of the Oak Ridge Seed Money program in 1974. I am encouraged by the results of the Oak Ridge program and have every confidence that these principles, now more broadly applied, afford a continuing opportunity for creative and highly productive research.

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Introduction

In 1974, a modest program for funding new and innovative research was initiated at the Oak Ridge National Laboratory. It was called the "Seed Money" program because of its emphasis on new ideas having potential for growth. Originally, it was unique among the United States Department of Energy's National Laboratories. Today, it is still in operation, but has since become part of a larger program, called Exploratory R&D, which is being carried out at all the Department's National Laboratories.

The creation of the Seed Money program was prompted by two observations in research. First, it was noted that many of the more exciting and productive scientific discoveries often arose unexpectedly in the midst of research focused on other objectives. While it was tempting to divert existing resources to pursue new ideas as they arose, frequently this was not possible. Previous commitments had to be met and discretionary funds were usually not available.

Second, it was observed that in large, mission-oriented research programs, such as those stemming from Congressional appropriations, new ideas and tangential pursuits, while meritorious, often had difficulty finding timely support among traditional program sponsors. Resources in the near-term were often already fully committed, or the idea itself was so new or tangential that it often fell outside of a program manager's primary area of responsibility.

Acknowledging that new ideas may have been overlooked as a result, the Department's Oak Ridge Operations Office, in collaboration with the Laboratory, established the Seed Money program to address this need. Under this program, the Department authorized the Laboratory to use a small portion of general operating funds for the purpose of "early exploration of creative scientific and technological concepts arising in the course of the Laboratory's work."

The Seed Money program's primary objective is to encourage the research staff, through the availability of special funds, to pursue new ideas and approaches. Of particular interest are promising ideas that either fall outside the scope of existing programs or demonstrate a unique proof-of-principle. Both serve as a means for attracting new interest and outside support for promising avenues of research.

In recent years, the Seed Money program has been funded at approximately $1 million per year. By the end of 1985, over 200 projects had been supported at an average cost of about $43,000 per project. The average duration of a project is about 1 year.

The program is managed exclusively by the Laboratory, including the evaluation and selection of proposals. Rotating appointments among the Laboratory's professional staff provide both the managers of the program and the scientists and engineers for peer review and selection of proposals. Selection criteria include the proposal's novelty, technical quality, and potential for continued funding. Each year, the approval rate has normally run about 60 percent, a rate that continues to encourage researcher interest and the generation of new ideas.

The Seed Money program, of course, operates within the larger and supporting environment of the Laboratory as a whole. This enables Seed Money researchers to make use of an extensive complement of unique facilities and resources available through the support of other programs. In this context, the accomplishments of the Seed Money program may be attributable, in part, to research support from others both prior and subsequent to each Seed Money effort. In a sense, this infrastructure provided both the Seeds and the nurturing environment in which the Seeds could grow.

Having set this context, the results of the program are impressive. Follow-on research, stimulated by successful Seed Money projects, has been prolific. Over 500 presentations have been made at technical conferences describing the results of Seed Money projects and their follow-on work. Over 400 manuscripts have been submitted for publication. Patents stemming from Seed Money research now number 11.

Research stimulated by the Seed Money results has produced 12 of the Laboratory's 46 IR-100 Awards. These awards are conferred annually by *Research & Development* magazine (formerly *Industrial Research*) upon the year's top 100 developments selected by experts from industry and academia. The IR-100 Awards recognize innovations in basic science that are likely to lead to inventions of great practical and economic value.

This report highlights 12 accomplishments of the Seed Money program. Each is a story of success. Their presentation here serves a number of purposes. One is to foster an appreciation for the work itself, for the difficulties encountered, and for the ingenious means by which problems were overcome. A second is to convey an understanding of the process of basic and applied research and of the environment in which it thrives, for therein lies the root of our technological advances and a source of future economic growth. A third is to increase awareness of the benefits of research, especially as the seemingly arcane discoveries of science become transformed into practical applications clearly appreciated by the public at large.

Finally, this collection serves as an illustration of how a relatively small amount of discretionary funding, combined with open competition among top-quality researchers, can be leveraged to great advantage. The Seed Money program has filled an important niche in the process of innovation, as the following stories show.

New Materials

Nickel Aluminide

Nickel and aluminum, when combined in a ratio of about 3 parts to 1, with trace amounts of boron added, can be formed into a unique metallurgical alloy with some extraordinary and useful properties. The development of this remarkable material, whose full potential has yet to be realized, was aided substantially by a research break-through in 1982 funded by the Seed Money program.

Nickel aluminide is much stronger than steel. In contrast to most other materials, it actually increases in strength in high temperature environments up to about 1300°F, and maintains its strength well above 1600°F. It is lightweight and highly resistant to corrosion by oxidation. It is malleable, making it easy to form into different shapes. Yet, with the addition of certain other elements, it can be made to resist strongly permament deformation and rupture at elevated temperatures, two common modes of metal failure.

While more expensive than ordinary steel, nickel aluminide promises to be highly cost competitive with other specialty materials, such as heat resistant alloys made of nickel, titanium, and vanadium.

The mechanical properties of nickel aluminide provide significant advantages over many currently available heat resistant materials in a number of economically important applications. These range from machine tools and boilers to parts for the automotive and aerospace industries. For example, at 1500°F, a temperature well within the operating temperature ranges experienced by most metal parts in today's gas turbines, jet engines, and diesels, nickel aluminide is four times stronger than high temperature steel.

Because of its high strength at these temperatures, the alloy is now being examined under exclusive license by Cummins, Inc., a major United States manufacturer of heavy diesel engines. An initial application under investigation is its use in strengthening exhaust valves. This part of the engine, which is subjected to high temperatures, corrosive environments, and repeated pounding, is often the first part to fail. Extending valve life with an improved material would increase the engine's reliability, stretch out maintenance schedules, reduce costs of repairs under warranty, and make the entire engine more competitive in international trade.

Because the alloy is made partly of aluminum, it is 10 percent lighter than steel. Also, because of its strength, a part made from the alloy can be designed smaller, further reducing its weight. Hence, the alloy has also generated considerable interest in the aerospace industry as a substitute for heavier materials now required for strength, such as fasteners, rivets, and certain structural components.

Another valuable property of the alloy is that once it has formed an initial, protective layer of aluminum oxide, it is nearly impenetrable to further corrosion and oxidation. Its corrosion resistance has been measured at 1000 times better than competing steels. As a result, it is now being investigated for use in heat processing equipment subjected to fouled environments, such as steam boiler tubes and hot exhaust gas heat recovery equipment in industry.

As a material, nickel aluminide is part of a larger family of materials known as "ordered" intermetallic alloys, so-named because of the precise ordering and interweaving of the atomic structures or lattices of the two metals. This particular situation, called a low "free energy" condition, makes it difficult to remove an atom from its position in the lattice, which gives the material its strength, or to have it react chemically with outside agents, which gives it its property of corrosion resistance. While these materials were well known in the 1950's and 1960's, the problem with them in the past had always been that they were too brittle for most practical applications.

Research funded by Seed Money in 1981 and 1982 set out to solve the problem of brittleness by applying newly acquired knowledge about the behavior of certain impurities positioned at the grain boundaries, or interfaces where different crystals in a material come together. It is at these interfaces where the crystals can slip against each other, causing the material to break.

The Seed Money experiments focused on increasing the adhesiveness at these slip surfaces. This involved varying the proportions of nickel and aluminum, mixing in small amounts of four different alloying metals to be used as the impurities, which would hopefully migrate to and lodge in the grain boundaries, and finally, testing a number of different metallurgical processes.

Through an extensive process of trial and error, guided by new theoretical models and data (see Positron Probe), the optimum combination came to be known. Nickel aluminide was made sufficiently ductile to fabricate successfully without degrading its other desirable properties.

This success, published in *Science*, was pivotal in the development of a whole new field of research on ordered intermetallic alloys. It precipitated much follow-on and continuing research by both Government and industry on nickel aluminide. As one measure of industry's interest, over a half a million dollars in research money was provided by the private sector to the Laboratory in 1985 to investigate related production and processing methods.

The research earned an IR-100 Award from *Research & Development* magazine and is now subject to extensive patent and licensing activity by private industry.

Ion Implantation

Since the dawn of the Bronze Age more than 5,000 years ago, when man discovered that copper mixed with certain amounts of tin could overcome the shortcomings of stone tools, there has been a relentless search to combine the elements of the earth in new and improved ways to better serve his needs.

This search took a dramatic turn with the advent several decades ago of a technology called ion implantation. This technology, named after the method by which it is accomplished, literally enabled the modern metallurgist to construct the operative surfaces of desired materials atom by atom.

Seed Money research funded in 1975 and 1976 played an important role in the further development and expanded commercial application of this technology. Although the technology had been demonstrated as early as World War II, and was already in operation in a number of limited cases, Seed Money research provided valuable insights and new understanding, which invigorated research by others and broadened considerably the scope of potential applications.

The power of this technology lies in its ability to construct precisely materials by design. It has long been known in materials science, for example, that small quantities of selected elements, or so-called impurities, when introduced into solids, can alter or even dominate the electrical, chemical, optical, and mechanical properties of the original material.

These properties, such as strength, hardness, resistance to corrosion, electrical conductivity, and others, often impose the crucial and limiting constraint upon further advances in technology. A material pushed beyond its limit may cause a larger device to fail. Hence, the search for improved materials, largely focused on the introduction of impurities and new combinations of elements, lies at the forefront of intense global competition among both users and suppliers of high-performance technology.

In this search for new materials, ion implantation is a powerful tool. It uses a variety of standard techniques for ionizing atoms, that is, removing electrons from the atoms of the elements to be implanted, and once the atoms are electrically charged as ions, uses an electric field to focus and accelerate them onto, and implant them into, the surface of the material to be modified. Once embedded in the material, the ionized atoms return to their neutral state.

This process can implant selected elements precisely at varying depths in varying concentrations. It is versatile. Virtually, any species in the Periodic Table of the Elements can be selected with almost absolute purity. It is highly reproducible, a crucially important factor in commercial applications.

Perhaps most importantly and uniquely, it is not constrained by solubility and equilibrium considerations of traditional metallurgy. Under these constraints, for example, tin must be soluble in molten copper in order to form bronze, or carbon in iron to form steel. But not all potentially desirable combinations meet these constraints.

Direct construction of materials by ion implantation, by contrast, allows the formation of new combinations of elements heretofore beyond our grasp, such as materials in supersaturated and metastable states. It can forcibly insert any number of atoms of one material into the underlying base structure of another, causing the atoms of both to interact in new and often unique ways.

With hundreds of researchers now working in the field, commercial applications are proliferating. Their initial successes have had a profound impact on new product development in high-tech industries, spanning health, aerospace, defense, computers, and others. Although the Seed Money research on ion implantation cannot be directly credited with these successes, it can be credited with producing new insights and fundamental knowledge upon which others built.

The primary focus of the Seed Money project was on the development of so-called metastable materials, wherein the concentration of implanted atoms of a foreign kind in a base material greatly exceed that allowed under normal solubility constraints. Such materials, it was hypothesized, might be used to create so-called superconducting materials, wherein the resistance to electrical current drops to zero under certain conditions, or very efficient solar (photovoltaic) cells, wherein sunlight is converted directly into electricity.

As is often the case in the path of research, the Seed Money success in this area was initially born of failure. The story of this success is also one of R&D leadership sensing an opportunity, pulling together the capabilities of equipment and human resources from different arenas, and moving quickly into new and uncharted territory.

In the summer of 1975, in anticipation of the arrival of a new piece of equipment, the leadership of the solid state research division at the Laboratory saw developing a unique confluence of technical capabilities. The new device was to be a low-energy, high-current ion accelerator, capable of manipulating a broad range of atomic species, or elements. This device would be used as the ion implanter. It was to be integrated with a complex array of other equipment, the most important of which included a high-energy positive ion accelerator with an ultra-high vacuum scattering chamber, which would be needed for diagnostics.

The combined capabilities of this facility would allow *in situ* creation and modification of precisely specified and varied materials through ion implantation. Simultaneously, they would provide a battery of sophisticated diagnostic tools, traditionally used in the fields of atomic and nuclear physics, such as Rutherford scattering, ion channeling, and electron transmission microscopy. Hence, the Seed Money researchers could probe the atomic structure of the created materials and analyze the results.

The Seed Money project provided an opportunity to study in fine detail the effects of ion implantation on the atomic structure of the underlying material under varying conditions. Importantly, it also allowed the temporary hiring of a visiting scientist from Australia, experienced in the use of ion accelerators, to contribute to the work and help build the technology base for further applications.

As mentioned earlier, the first part of this effort resulted in failure. While the ion implantation objectives were met, namely, the specified materials had been exquisitely constructed with higher purity, greater concentrations, and more homogeneity than previously attainable, neither material performed as expected.

The ensuing investigation of the detailed atomic structure of the material revealed the reason why. Extensive damage had been done to the crystal structure of the underlying base material as the ions had been implanted. This necessitated a heat treatment process to repair, or anneal, the damage. But the process of heating the material in the oven (bulk-mode heat treatment) allowed the excess atoms to escape (precipitate), thus destroying the sought after metastable or supersaturated condition.

This finding pointed out the limitations of bulk-mode heat treatment. It also set the stage for the successful search for an improved annealing process, (see Laser Annealing), one which might be carried out in a flash or pulsed-mode so quickly that the atoms did not have time to escape.

This is in fact what happened. Using laser annealing, the researchers were able to create a new solar cell, which at the time set unprecedented records of efficiency. The study of the damage and the use of the laser created enormous excitement in the field. The laser's fast pulse and precise control over depth of penetration provided a means for both studying structural damage in detail and overcoming (repairing) a key problem (structural damage) which had limited ion implantation's more broadened application. Based, in part, on the knowledge stemming from the use of such methods, ion implantation, in conjunction with laser annealing, became an exploding field of research and a growing commercial venture.

The underlying research performed by this Seed Money project unveiled to the scientific community a deeper physical understanding of ion implantation as a means for creating and modifying materials. It also highlighted the unique combination of diagnostics available at the Laboratory and the valuable insights that could be gained by their use. These insights helped other researchers in commercial firms pursue their own developments. Today, ion implantation, apart from laser annealing, is a thriving and expanding industry.

Research at the Laboratory, for example, performed as an extension of the initial Seed Money project, found that the implantation of nitrogen in the surface of surgical bone implants made of a titanium, aluminum, and vanadium alloy, reduced wear rates by a factor of 400. This proportionately increased the implant's practical life. Prior to this, implants were not generally used for patients with more than 10 years left to live, because they would wear out, breakdown, and cause internal poisoning.

Spire Corporation, a Bedford, Massachusetts firm, has manufactured hundreds of nitrogen implanted hip prostheses for a major health product manufacturer currently performing clinical trials. Potential applications for hip joint replacements and other purposes are estimated at 150,000 per year.

The United States Navy contracted with Spire to develop hardened metal bearings for high performance jet aircraft engines. Implantation of common steel with chromium, molybdenom, and boron or alternatively, titanium and carbon has been found to double or triple bearing life, as well as make their manufacture more uniform.

Similar applications are now being pursued to improve the performance of metal working dies, punches and cutting tools, such as those used to stamp out the precision cuttings in the top of a soft drink can to make the pull tab work. New dental drills and burrs are being designed, with the hope of making trips to the dentist a painless experience. Spinneretts, which are nozzles used to extrude glass or organic polymer fibers and are made of cobalt superalloys or chromium carbide, have been treated with silicon, titanium, boron and other ions to reduce deformation under pressure and oxidation of their surfaces, two common modes of failure.

Even organic polymers are being modified with ion implantation processes to give them certain electrical properties, heralding the potential advent of plastic electrical wires. Ceramic materials, which are known to have extraordinary resistance to high temperatures but are usually too fragile for reliable use, are being treated with ions of chromium (another Seed Money project) to make them superhard and less prone to fracture and wear.

Proposed applications of ion implantation are simply too many to enumerate. The current state-of-the-art must be credited to literally hundreds of researchers around the world who have made important contributions.

The Seed Money research in 1975 and 1976, however, may be credited with establishing the basic research program at the Laboratory that gave rise to renewed and broadened interest in ion implantation, and also to the unique combination of ion implantation and laser annealing. It also provided the technology base for many subsequent advances at the Laboratory and elsewhere. These early breakthroughs, published in *Science*, heightened worldwide interest in related technologies, which led to an avalanche of applied research and commercial product development.

Laser Annealing

Today, the unique capabilities of laser technology are being applied to selected manufacturing processes in ways that have significantly reduced costs and improved product quality in some of America's most important and fastest growing industries. The laser's capability to deliver an intense concentration of energy in the form of light with surgical precision, for example, is now being used to heat treat or "anneal" the microscopic metal surfaces of semiconductors, the basic components of microprocessors and computers.

This process, called laser annealing, and a related process, called rapid thermal annealing, involve the rapid heating and cooling of a microscopically thin layer near the surface of the material. The process eliminates thousands of both naturally occurring and manufacturing induced defects and, in the case of semiconductors, improves dramatically electrical performance. It also eliminates the need for cumbersome and potentially damaging furnace-type heat treating of the entire part, speeds the manufacturing processes, improves product uniformity, and lowers production costs.

The origin of laser annealing can be traced to a seemingly unrelated Seed Money project funded in March of 1975. The focus of this research was on increasing solar cell performance by improving the distribution of phosphorus in crystals of silicon, a combination of elements which gives rise, in part, to the unique and valuable properties of semiconductors. Conventional methods of manufacture typically result in unevenness in the distribution of phosphorus, called inhomogeneities, which adversely affect electrical performance. The technique proposed to solve this problem took advantage of certain fundamental nuclear relationships between the elements of silicon and phosphorus.

As it appears in nature, there is a natural abundance of about 3 percent of one particular variety of silicon, called Si^{30}, an isotope which is slightly heavier than silicon's other naturally occurring isotopes (Si^{28} and Si^{29}). With the addition of one neutron from a nuclear reactor, however, Si^{30} becomes Si^{31}, which shortly thereafter decays to a stable (i.e., nonradioactive) isotope of phosphorus, P^{31}. Hence, neutron activation of silicon presented a means of evenly distributing phosphorus, *in situ*, after the silicon crystal had been formed.

With funding provided by the Seed Money program, this line of research, called neutron transmutation doping (NTD) of silicon, was pursued successfully. NTD silicon has a number of critically important applications in the transmission of high voltage power in rectifiers and thyristors, in certain defense applications, such as in infrared detectors and other devices, and in the field of nuclear science as sensitive radiation detectors.

Fortuitously, as later events proved, the funding also allowed the temporary hiring of a young scientist, Rosa T. Young, to help out on certain aspects of the work, namely, the fabrication of the solar cells into a working device. She concentrated on one important step in the process of modifying materials by particle bombardment—the repair of the damage done to the crystal lattice structure of the original material by the impinging particles.

Standard practice was to heat, or anneal, the modified material in hot ovens for hours at a time. In the case of NTD silicon, this process worked adequately in repairing some types of damage, but not all types of damage.

Frustration with conventional annealing processes led Rosa Young to request a comprehensive, worldwide literature search of alternative methods. This search uncovered a single citation on laser annealing in a Russian physics journal.

Motivated by this suggestion, Rosa tried a number of different types of lasers available at the Laboratory, all of which failed, until she struck upon a ruby laser borrowed from the Laboratory's fusion energy research division. With a single pulse lasting only 50 billionths of a second, she was able to repair virtually 100 percent of the structural damage in her sample materials, enabling them to become semiconducting at unprecedented levels.

Follow-on research revealed a number of important advantages of this new process over thermal annealing in a furnace. A principal advantage is that the laser light is heavily absorbed only in the thin surface layer of the solid. This produces very high temperatures (even melting) in the surface region, which are necessary for annealing the lattice damage. Yet, the absorbed energy is insufficient to raise the temperature of the undamaged substrate significantly. This avoids the deleterious effects of high temperatures in the rest of the part, such as warping and localized deformation, associated with bulk-mode heat treatment methods.

Another advantage for some applications is that laser annealing can be carried out in ordinary air, rather than vacuum, because the surface region subjected to high temperatures cools so rapidly that introduction of significant amounts of impurities from the atmosphere is minimized. This feature is particularly attractive for highly automated device fabrication.

Research stemming from these initial studies eventually led to six patents for the improvement of the properties of semiconductor materials, to an IR-100 Award, and to solar cells with efficiencies comparable to those made by the most complex conventional manufacturing procedures.

Although the focus of the Seed Money research was on solar (photovoltaic) cells, the scientific knowledge gained in developing laser annealing, proved to be of even greater value to manufacturers of advanced electronic microcircuits and computer chips. Pulsed laser annealing consists of exposing prepared materials to extremely short pulses of laser light. Lasers were chosen because they allow precise control of the extremely high intensity light required for the most complete annealing. However, from the theoretical and experimental framework developed to describe the laser process, it became apparent that certain conventional sources of light and heat could be substituted for lasers to obtain annealing results suitable for a number of applications.

Industry built upon these insights gained at the Laboratory and other laboratories, finding that arc lamps and high-intensity halogen lamps provide annealing nearly comparable to that obtained with conventional furnaces and at greatly increased rates. The commercial process has become known as rapid thermal annealing.

Sales of rapid thermal annealing equipment have grown in volume from $100,000 in 1979 to $10,400,000 in 1984 and are projected by industry sources to continue to grow rapidly over the next 5 years. The laser industry is following the developments in the field of laser processing with keen interest and several lasers specifically designed for laser processing of semiconductors are now on the market and selling well.

The technological applications of the new processing techniques are of great importance, but it may be that the opportunities they have provided for the study of fundamental problems in materials science are of even greater long-term significance. For example, the pulsed laser melting of doped semiconductors is followed by resolidification at rates much greater than those that can be obtained by any other methods. This has not only allowed detailed studies of how the atomic structure of a liquid is transformed into the structure of a solid, it has also provided a practical means (see Ion Implantation) for making totally new materials whose properties are now being intensively studied.

Better Health and Environment

Burn Meter

Hospitals in the United States typically report 250,000 cases of burn injuries each year, 20,000 of which are serious enough to require hospitalization. Yet, even in this day of modern medicine with its advanced technology, the examining physician is woefully equipped to diagnose the extent of the more serious burns and prescribe the proper treatment. This situation may soon be reversed.

Today, based on research funded by the Seed Money program, a prototype machine, called an ultrasonic burn diagnostic unit, or burn meter, is under development for use in clinical trials. The significance of this development and its implications for medical treatment may be appreciated by understanding first, second, and third degree burns.

A first degree burn involves only the outer layer of skin, the epidermis, and causes blistering. Although burned and blistered, the skin remains capable of preventing infection and healing normally.

A second degree burn damages the second layer of the skin, the dermis, which contains nerves and blood vessels, and causes swelling below the epidermis. The prognosis for a second degree burn depends on the depth of the injury and whether infection occurs. Shallow second degree burns eventually heal by themselves. Deep second degree burns are more easily infected, and treatment may require removal of the burned tissue and replacement with skin grafts.

A third degree burn destroys tissues in the layer below the dermis causing blood clots, swelling, accumulation of body fluids, and a high susceptability to infection and blood poisoning. These burns almost always require removal of the dead tissue before it causes blood poisoning, and replacement with skin grafted from other parts of the body.

In serious burn cases, it is crucial, however, not to remove too much skin. If the burn area is extensive, donor skin sites may be limited and should be used sparingly. The use of skin grafting in the case of second degree burns capable of self repair should be avoided. Moreover, too much skin removal may produce unacceptable shock to the patient.

Hence, in the case of deep second degree burns, the examining physician is faced with a dilemma. Relying primarily on superficial observation, a method known to be highly imprecise and often misleading, a crucial assessment must be made of the extent of the burn and its prognosis, and whether or not radical treatment is required.

No widely used technique has been found that consistently diagnoses these cases. Several weeks may elapse before a clear demarcation emerges between second degree burns that will heal and those that will not. Delay enhances the probability of irrevocable blood poisoning and death. Early knowledge of the depth of injury would aid diagnosis and might preclude unnecessary and risky surgery.

In 1975 researchers funded by the Seed Money program laid the scientific foundation that now offers hope for a solution to this problem. Based on this research, a prototype machine, now under development for use in clinical trials, makes use of harmless sound waves, in a fashion similar to sonar, to probe the condition of the skin and its underlying tissues. Within minutes, it makes highly accurate quantitative measurements of burn depth. It also produces a clear, cross-sectional picture of the various layers of the skin, enlarged about a hundredfold, and provides the physician the essential information needed for a correct diagnosis.

Although ultrasound techniques are not new, the problems faced by the Seed Money researchers were most difficult in several areas. First, they had to work within extremely shallow depths. The average thickness of the human skin is only about one milimeter, or about 1/32 of an inch. Second, they had to devise a means of distinguishing the subtle acoustic differences between normal tissue and recently burned tissue, wherein the more telling characteristics of dead tissue are not yet set. Also, they had to find a way to overcome a nearly blinding reflection of the original sound wave, the so-called main bang echo, as it bounced off tissues in the body other than those of interest.

Using samples of tissue burned in varying degrees, and comparing the results of microscopic analysis to ultrasound data, they investigated a number of different approaches to overcoming these difficulties. Ultimately, they determined that certain ultra-high sound frequencies could yield the resolution required within the shallow depth. They devised a means for subtracting out the main bang echo. And they employed a clever mathematical technique, called Fourier transforms, to process the returned signals and distinguish between the healthy and burned tissue.

These early successes demonstrated the feasibility of burn depth measurement by means of ultrasound, and paved the way for subsequent technology development. The results were published in numerous technical journals, including *Medical Physics*, *Journal of Trauma*, and the *Journal of the Acoustics Society of America*.

Their research and the resulting device won an IR-100 Award from *Research & Development* magazine and was granted a U.S. patent. NASA sponsored subsequent development and testing of the prototype unit. It is being built under a licensing agreement with Advanced Technology Laboratories of Seattle, Washington. Its clinical trials are scheduled to take place on burn patients at the hospital and medical school of Virginia Commonwealth University.

If successful, this machine could revolutionize burn diagnostics in the hospital emergency room. When needed, early removal of burned tissue, often recommended reluctantly in borderline cases, can reduce mortality, promote earlier wound closure, and reduce deformaties. Armed with knowledge of where the precise interface occurs between burned and healthy tissue, the physician can make well informed judgements about patient prognosis and prescribe the correct treatment. Aided by such a machine, the burn patient of the future could look forward to less physical trauma, a shorter hospital stay, and a more rapid return to normal life.

Legionnaires' Disease

In August of 1976, a mysterious and frightening disease was visited upon the American Legion convention at the Bellevue-Stratford Hotel in Philadelphia. One by one, conventioneers became fatally ill with flu- and pneumonia-like symptoms for which there was no known cure. The hotel was closed; but before it was over, 29 people had died.

Months later, the cause of what came to be known as Legionnaires' disease was isolated from autopsied tissues by microbiologists at the Center for Disease Control in Atlanta. It was found to be a form of bacteria, classified and named *Legionella pneumophila*. *Legionella* have since been found to be present in minute amounts in almost all fresh waters.

Normally, this form of bacteria is relatively harmless. Under certain conditions, however, it can become deadly. Tragically, the disease struck twice more in the warm weather months of 1977 at hospitals in Burlington, Vermont, and Los Angeles; and more people died.

Today, there is a cure for Legionnaires' disease. If properly diagnosed, it may be treated with a readily available antibiotic called erythromycin. Yet, for years following these incidents, crucial aspects of the disease remained a mystery.

Why did the disease seem to strike so selectively in hotels and hospitals, and seemingly most often in the warm weather months? How could relatively harmless bacteria, found in almost all fresh waters, become so infectious and dangerous? Since *Legionella* normally exist in low concentrations, what caused them to proliferate? Most importantly, how could the tragic events of the past be prevented in the future?

Results from Seed Money research, funded in three separate projects in 1976, 1983, and 1984, as well as from follow-on research funded by others, played a key role in answering some of these questions. Owing, in part, to this work and to that of other scientists working on the problem, a fairly clear picture of the disease and its underlying causal factors has since emerged.

Under normal circumstances, the bacteria are not dangerous to man, even if swallowed. This is particularly true if they remain in their usual state of low concentration. They do become dangerous, however, if they begin to proliferate wildly and if they happen to gain entry into the lungs.

A common route of entry into the lungs was found to be from inhalation of airborne mist. Such mists can arise from shower heads, building air conditioning systems in large hotels and hospitals, and cooling towers associated with certain types of large industrial plants and electric power generating stations.

Concerning proliferation, Seed Money researchers, working on a problem unrelated to *Legionella* at the time, discovered a means by which the bacteria might multiply themselves more than a millionfold. Their study in 1976 focused on the effects of heated waters on the growth of two varieties of one-celled organisms, called amoebae, namely *Naegleria* and *Acanthamoebae*. These organisms attack bacteria and consume them as food. In consuming *Legionella*, however, the amoebae can become infected with the disease and act like factories producing prolific amounts of the bacteria. In this way, high concentrations of *Legionella* were linked, in part, to the presence of amoebae.

Further, Seed Money researchers found that these two varieties of one-celled organisms shared an ability, as do *Legionella*, to tolerate and, in some cases, thrive in heated waters. In natural settings, amoebae populations peak in the summer months. In cold waters, by contrast, their concentrations are much less.

Thus, Seed Money research provided a plausible explanation of why Legionnaires' disease is associated with the dispersion of waste heat by means of building air conditioning systems and industrial cooling towers. Concentrations of disease producing organisms, including both amoebae and *Legionella*, may be amplified by heated waters. In addition, *Legionella* may be further and dramatically amplified by the presence of amoebae. Finally, the physical operation of cooling systems provides two aggravating conditions, namely the heated waters and the pathway into the lungs via airborne mist.

In another Seed Money project in 1983, researchers focused on the implications of this earlier work and found evidence of certain occupational risks associated with Legionnaires' disease. They examined blood samples taken from workers who cleaned cooling towers at electric power plants. Testing for the presence of antibodies associated with the disease, they found evidence that as high as 40 percent of the workers at some locations had been exposed.

The utilities in question took immediate and corrective action. Although the problem was corrected, the discovery of its existence underscored the need for more broadly based monitoring of similar situations. Further, the 1983 research showed that the amoebae and the bacteria could both be controlled with special chlorination techniques, pointing the way toward effective prevention programs.

Following up on the need for monitoring, Seed Money researchers in 1984 developed a fast and economic method of testing for Legionnaires' disease. While their method makes use of commercially available equipment and standard procedures in a technique called flow cytometry, this was the first application of this technique to Legionnaires' disease. Their method works on both clinical (blood) and environmental (water) samples and can positively identify the presence of *Legionella*, thus serving as an effective warning and screening technique.

In sum, as a result of these three Seed Money projects and their follow-on work, high risk areas can now be clearly identified. The availability of reliable methods for clinical and environmental testing is helping to minimize both occupational and public health risks of exposure. Importantly, the improved understanding of *Legionella* and the environmental factors affecting their growth has set the stage for the development and implementation of improved preventive and control measures.

Whole Body Radiation Counter

Since the earliest days of atomic energy, understanding the health effects of human exposure to radioactivity and minimizing the risks of associated occupational hazards have been of paramount importance to all involved. Routine monitoring, extensive precautions and decades of health effects research are hallmarks of the industry.

Yet in the case of uranium and other classes of the heavier manmade elements, one of the most difficult clinical problems is the accurate assessment of a person's cumulative exposure to these elements. While exposure may be inferred roughly from circumstances, external monitors, and medical records, an assessment using such methods is uncertain. Until recently, there existed no means of direct measurement.

In 1975 and 1976, however, Seed Money researchers laid the foundation for the development of a sophisticated diagnostic instrument, which later became the standard of the industry. Today, three private firms manufacture the instruments, called whole body radiation counters, and more than 20 of them are placed in key locations throughout the country.

These instruments are now used routinely in the precautionary screening of thousands of workers and researchers. They monitor the exposure history of each individual and can spot any new developments. The reliability of the machines, combined with the accumulating reports of a clean bill of health, lend confidence to both the workforce and the professional experts concerned with the safety of the work environment.

In the event of an accident, these instruments can provide rapid, accurate, and detailed information on the nature of the exposure. Such information is essential in determining the seriousness of the problem and prescribing the proper treatment. The instruments can then monitor treatment progress and the subsequent removal of the radioactivity from the body, ensuring that it does not become entrenched or concentrated in sensitive areas.

Aside from the development of this technology, the underlying research associated with this work resulted in many other valuable contributions to the broader field of health physics. The methods and data, original to this effort, improved the means by which assessments are made of the impacts on the environment of all aspects of the nuclear fuel cycle, from uranium mining to the disposal of waste. The results are also important to the development of nuclear safeguards, handling of special materials, and research into a host of biomedical applications used in the treatment of common diseases.

The nature of this achievement may be appreciated by understanding a few of the technical details. In many cases of exposure, the most common route of entry into the body of the heavier radioactive elements, more formally called transuranic nuclides, is via the respiratory system. Typically, they take the form of dust, attach themselves to fine airborne particles, or to minute droplets of water, such as found in condensing steam. As such, they are inhaled and deposited, mainly in the lungs.

An accurate medical assessment of this situation requires precise knowledge of the type and quantity of each nuclide deposited, of which there may be more than a dozen. Once deposited, however, they are very difficult to detect. This is because most of the telltale signs that would otherwise arise from the radioactive elements are either fully hidden by the surrounding tissues or of such weak or varying strengths that they cannot be uniquely identified using conventional radiation detectors.

In the natural course of the radioactive decay of a heavy element, however, there is a faintly detectable secondary reaction, which gives rise to the emission of a number of low energy x-rays. The emissions from this secondary reaction provided the key to the information the Seed Money researchers were seeking.

Technically speaking, as the nucleus of a large and unstable atom transforms itself into a slightly smaller one, in a process called decay, it gives off among other things an energetic, electrically charged (alpha) particle. This type of emission forms the bulk of the radioactivity.

In many instances, however, the newly formed nucleus is left in a highly perturbed or excited state. In a nuclear process called "internal conversion," this extra energy may be transferred to one of the nucleus' orbiting electrons. This causes the electron to become excited, knocking it out of its normal or so-called ground state. The resulting "hole" is then filled by a neighboring electron, which falls into the hole, creating a new one, and gives off an x-ray in the process.

As this process is repeated, the cascade of falling electrons gives off a wide range, or spectrum, of low energy x-rays. The characteristics of the spectrum are unique to each nuclide and are akin to an identifying signature or fingerprint. Some of these x-rays pass out of the body unobstructed and, in theory, could be detected.

The Seed Money researchers reasoned that if they could develop a detector of sufficient sensitivity to count the x-rays, and of sufficient power of resolution to finely measure their identifying energies, then they could work back through the reference data on x-ray spectra and determine all the contributing sources.

Although seemingly straightforward, there were several problems to overcome. The x-rays were so weak that a highly sensitive, wide-area detector had to be built and calibrated. Second, reference data for many of the manmade elements were either uncertain or did not exist. The researchers had to confirm them or develop them from scratch. Third, the detected signal from one element appeared among the data with all the others. Like a complex puzzle, each piece had to be carefully examined, matched with others, and then each matched set sorted out one-by-one. Overcoming all these problems, they were able to identify the sources.

Determining their quantities, however, was another matter. This is because the strength of the signal varies with the depth of the source and the extent to which the x-rays might have been obstructed by absorption in the body's tissues. Since these facts were not known, the quantity of each nuclide could not be inferred from the strength of the signal alone.

The solution to this problem involved a combination of physics and mathematical modeling of the body's tissues. The physics made use of the fact that the likelihood of an x-ray being absorbed by the body is roughly proportional to its energy. Typically, the lower the energy, the higher the rate of absorption. Hence, a comparison of two or more different x-rays from the same nuclide, each having a discrete energy, should show a proportionally greater fall-off in signal strength among those at the lower end of the energy spectrum. The extent of this fall-off reveals crucial information about the depth of the underlying tissue and its absorption characteristics.

The mathematical modeling provided a three-dimensional picture of the body's bone, lung, and muscle tissues, each of which absorbs x-rays in varying degrees. By fitting the detected signal to the mathematical picture, and by comparing the expected values of absorption to the apparent values, the model could estimate the average depth of each source at each location, and calculate the amount of each nuclide present.

The Seed Money researchers developed the theory, data, and methods necessary to overcome each problem. The success of their experimental work proved the viability of the concept. This ultimately led to the development and commercialization by others of a highly sensitive, workable and reliable instrument.

Today, thanks to the existence of the whole body radiation counter, any individual who suspects that he or she may have been exposed to radioactivity from uranium and related manmade elements can be assured of an accurate medical assessment of the situation. With reliable information, a prognosis may be made with confidence. Importantly, the psychologically debilitating effects of uncertainty, which often accompany such cases, may be eliminated altogether. Treatment, if required, can proceed in a carefully deliberated fashion with increased likelihood of success.

The Anflow System

In 1974 and 1975, Seed Money researchers developed a new, highly efficient flow-through system for processes that use microorganisms, or bacteria, to convert organic matter into more beneficial products. Two common examples of such processes are the fermentation of grain into beer and the processing of municipal waste into clean water.

The new system, called ANFLOW, performs such functions more quickly and less expensively than conventional methods. Two important factors contributing to these advantages are the use of a special class of bacteria, called anaerobic bacteria because they live and thrive in the absence of oxygen, and the use of a steady-state, continuous flow method of processing. ANFLOW derives its name from the two words anaerobic and flow.

In bioconversion processes, continuous flow systems have long been known to have a number of advantages over so-called batch methods. Unlike continuous flow systems, batch methods require containment of the organic matter and the bacteria in large fermentation vessels or vats for long periods of time. Such methods tend to be slow and occupy large amounts of space. They require expensive machinery and monitoring instruments. They also consume large amounts of energy in maintaining precisely controlled temperatures and environments as the biological reactions take place over time in increasing concentrations.

The ANFLOW system, by contrast, processes organic matter in a continuous, steady-state mode of operation. It is inherently simpler and occupies less space. It exhibits higher yields, produces less by-product waste, and reduces processing time from days to a matter of hours.

Although the ANFLOW system, since patented, is a generalized one with many applications, one of its first uses was to convert municipal wastes into a harmless effluent suitable for discharge into rivers and streams. Laboratory testing showed that the ANFLOW system treated sewage at higher loading rates than the prevailing activated sludge process.

Technically speaking, the ANFLOW system is an upflow, packed-bed bioreactor. Prior to its development, there had always been a number of serious difficulties in using anaerobic bacteria in flow systems.

Seed Money researchers overcame these difficulties in two ways. First, they made use of an upflow, packed column of organic liquids to keep the biosystem free of air, using a concept first developed at Stanford University. Second and importantly, they developed a special packing material and coating.

The combination of the special packing material and coating immobilized the microorganisms so that they did not flow out of the system as the organic matter passed by. Also, it enabled the researchers to control the rate of bacterial growth, which optimized efficiency and kept the system from clogging. Finally, the packing material greatly expanded the available surface area inside the bioreactor. This increased the production yield and reduced the concentrations per unit surface area of certain chemicals in the waste stream that otherwise might kill the functioning bacteria.

Pursuing this line of research, the Seed Money researchers investigated several methods by which the live cells could be fixed or immobilized in the packed bed. They coated small ceramic shapes, such as saddles, rings, or glass spheres, each about the size of a grain of sand, with an adhesive material called a polyelectrolyte, and loaded them into the column. The polyelectrolyte was then chemically activated and cross-linked to form an interconnected structure that trapped microorganisms on its surface and accumulated them in the packing spaces.

Laboratory tests showed that, as a result, the bacteria remained healthy and intact (immobilized) as the process stream passed over the surfaces and through the packed bed. Biological activity increased. After 2 years of successful operation, no clogging had occurred.

This success paved the way for the advancement from batch type bioconversion processing to continuous flow type systems in a wide range of other applications. In one experiment, the ANFLOW system increased the conversion efficiency of glucose to ethanol (grain alcohol) by 50 percent over conventional methods.

ANFLOW has also been tested and showed promise in a number of other areas. These include: converting organic wastes to fuel gas, converting cottage cheese whey to lactic acid, processing coal liquefaction wastes to remove dissolved carbon, breaking down cellulosic products into glucose, and converting methane into methanol (wood alcohol).

Moreover, the utility of the ANFLOW system itself may be further and dramatically increased by the availability of improved anaerobic bacterial strains. This is a line of research that has been encouraged by the above developments.

Two ANFLOW units have been installed and operated. The first was a 5,000 gallon per day (GPD) waste treatment pilot facility in Oak Ridge, Tennessee. This project benefited from the participation of the Norton Chemical Company, a private firm interested in the commercial development of the ANFLOW system. This installation helped Norton meet waste water discharge standards with a highly efficient and economic process.

A 50,000 GPD plant was built in Knoxville, Tennessee, and operated in 1980 and 1981 by the city of Knoxville and the Department of Energy. Glitsch Manufacturing Company provided the ceramic rings for packing the bed. The unit successfully demonstrated process scale-up, treating both municipal and industrial wastes.

Attracted by these successes, follow-on funding from a number of other sources enabled the continued technology development. A new firm, ANFLOW, Inc., has since been formed at Oak Ridge to market the system for waste treatment and other uses. A major ANFLOW project for the treatment of muncipal wastes is under construction at Haleyville, Alabama.

These practical applications, as well as the technological potential for transforming other bioconversion processes from batch to flow-through systems, owe their existence to the scientific work funded initially by the Seed Money program. The underlying research earned an IR-100 Award from *Research & Development* magazine and resulted in two patents.

New Scientific Understanding

Genetics and Molecular Biology

Ever since the Nobel Prize winning discovery in 1953 of the essence of life, embodied in the structure of a complex molecule known as DNA (deoxyribonucleic acid), there has been an explosion of scientific knowledge that is utterly transforming the study of life sciences and the practice of the healing arts.

Every form of life, including all plants and animals from human beings to the simplest bacteria, springs forth from DNA. A full strand of DNA, resident in each cell of its living host, contains the complete genetic code, or blueprint of life, that fully describes every biological aspect of an organism's existence. The precise sequence of the code determines its size and shape, strengths and weaknesses, functions and behavior. The living organism is, in essence, the ultimate physical manifestation of its underlying code.

Today, hundreds of scientists from plant biologists to cancer researchers are working both to determine the sequence of the code and to understand its meaning. Their hope is to identify the functions associated with its myriad arrangements and develop the tools needed to transform this knowledge into practical use.

Already, initial successes have brought enormous benefits. Rare forms of some human hormones, for example, can now be manufactured cheaply in the laboratory. Insulin used in the treatment of diabetes is perhaps one of the more dramatic cases. In other cases, with sufficient knowledge and capability, it may be possible for mankind to emerge triumphant in the future over some of its oldest and most dreaded scourges.

Although the promise for success is bright, the magnitude of the remaining task is staggering. The full strand of human DNA, called the human genome, consists of 3.5 billion elements of precisely sequenced genetic code. While the tools for analyzing such a complex molecule have improved dramatically in recent years, any hope of accomplishing the ambitious goal of complete understanding lies well beyond our current means. Smaller steps along the way must be taken first.

Hence, the focus of much of today's research is on smaller, more specialized and prioritized aspects of the larger problem. The object is to reveal in theory important lessons bearing on the whole, while addressing in practice a tractable set of research tasks.

Exemplifying this approach, Seed Money researchers in four separate projects funded in 1975, 1979, 1982, and 1985, played a fundamental role in developing basic knowledge in one particularly important, yet elusive area of investigation.

While it is well known that DNA provides both the code and the instructions for the manufacture of proteins, which are essential chemicals that stimulate and carry out an organism's vital functions, it is not known what causes the protein manufacturing process to start or stop. The focus of these four Seed Money projects, each being quite different from another, was on understanding the regulatory mechanisms that control the timing and duration of this manufacturing process.

To improve their chances for success, the Seed Money researchers chose for study a biological function associated with periodic and rapid growth of tissue, and selected an animal in which such behavior could be readily manipulated in the laboratory. The animal was a species of crab that normally lives out of water on land, and is fairly easy to maintain in captivity. Importantly, much of the DNA of this crab was known to break up under certain laboratory conditions into segments of interest that were of a manageable size (each of several thousand coded elements).

The biological function chosen was a process familiar to almost all fishermen, called molting.

Molting occurs when the crab begins to shed its old shell, either because it's damaged or too small, grows an underlying new and soft shell, enlarges it after the old shell has been discarded, and then gradually hardens it to complete the process. Conveniently for the purposes of research, molting can be initiated artificially in the laboratory.

Hence, molting is an important phase of growth. In fact, in the case of crabs, molting is the only time in which growth occurs. This enables investigators to compare genetic activities in growing and nongrowing periods, and draw important lessons from the differences.

Molting is an important focus of research for other reasons. It is biologically similar to the skin shedding processes of insects as they grow from larvae into adults in a process known as metamorphosis. Thus, it is a major focus of agricultural and environmental research aimed at controlling pests and understanding the effects of pollutants on life cycles and reproduction.

Also, the switching on and off of rapid tissue growth is of great importance to cancer researchers. One hypothesis for the cause of cancer is that a gene, vital to the beginning of life during the rapid growth phase of the embryo but normally dormant thereafter, is switched on again by cancer causing agents. A better understanding of the mechanisms that regulate rapid tissue growth might lead to a means for turning off such growth when it is not desired. This would be a direct and powerful cure for cancer, much more so then the less specific means of chemotherapy and radiation in use today.

In 1985 Seed Money researchers accomplished an important step along the way toward a better understanding of animal growth and growth-regulating functions. They culminated a decade of painstaking research by successfully identifying several proteins specifically associated with the crab's molting process.

This step is important because once the protein has been identified and isolated, researchers can use a number of standard laboratory techniques, working backward, to create an exact duplicate of the original DNA which gave rise to the protein in the first place. Once this DNA is in hand, it can be analyzed to reveal the sequence of the coded elements of the gene. Attached to this gene, researchers hope to find the switch that turns on the rapid tissue growth associated with shell replacement. This latter effort is now the subject of further research funded by others.

When decoded, the DNA sequences can be entered into a massive computerized library and compared to all other known DNA sequences. In this way, the keys to the regulatory functions in other species of animals may be revealed by association.

While the identification of the proteins is a major success, none of this line of research would have been possible had it not been for earlier work. In 1982, for example, Seed Money researchers used more classical biological techniques to isolate certain chemicals in the crab, called growth-regulating hormones, the fluctuating quantities of which were found to be closely correlated with the crab's molting stages. This success provided an important clue as to when and where to start looking for the proteins and set the stage for 3 years of non-Seed Money research. This subsequent research ultimately pointed the way toward the new and successful avenue of investigation pursued by the Seed Money researchers in their 1985 work.

The 1982 research, in turn, was made possible by earlier successes. Working on simpler segments of crab DNA, Seed Money researchers in 1975 were among the first anywhere to decipher correctly a segment of genetic code from higher order animals. In 1979 they established successfully at the Laboratory the methods and procedures for DNA cloning, or amplifying, a segment of a DNA molecule into more abundant and chemically useful quantities. It was these Seed Money projects that first brought together at the Laboratory the skills, equipment, and resources necessary to carry out sophisticated research in molecular biology and established the foundation on which the present work is based.

While the ultimate goal of this line of research has yet to be fully realized, and while the successes described here are not particularly unique in the burgeoning list of accomplishments in the field, these four projects collectively are representative of both the larger body of work and the process by which fundamental knowledge in this field is advanced.

Ten years of painstaking and meticulous research were required to establish the capabilities, perform the underlying research, and bring the resulting products to fruition. Each additional effort built on the successes of its predecessors.

These projects also serve as an example of how the benefits of basic research often come into clearer focus retrospectively than was possible at the outset. In 1975 it was not entirely clear to what practical end the Seed Money investment in DNA sequencing would lead.

Funds from the Seed Money program were used judiciously as a means of pursuing a new line of work and incorporating the latest scientific developments and techniques into an established organization more familiar with classical approaches. A few periodic and relatively minor Seed Money investments provided essential and nurturing support at crucial times to help establish a new avenue of research. With newly established credentials, each success led to subsequent grants from outside funding organizations. As a result, biological research at the Laboratory is now well positioned within the midst of a broad scientific revolution.

High-Voltage Equipment

The safe and efficient handling of high-voltage electric current is becoming an increasingly important issue in the development of advanced energy and defense technologies. As scientists and engineers begin to press the limits of today's high-voltage equipment, there is a crucial and growing need to better understand the fundamental interactions of strong electric fields, currents, and voltages with the materials and substances used to control them.

In the electric power industry, for example, there are compelling economic motivations to reduce the amount of energy lost in the transmission and distribution of electricity from the power plant to consumer. The amount of electricity lost is estimated to be on the order of 10 percent of total sales, valued in terms of today's prices at about $15 billion per year.

The principal strategy for solving this problem is to reduce the electrical current and its associated losses by increasing the voltage. A doubling of the voltage halves the current, which in turn reduces the losses due to electrical resistance by a factor of four. Hence, with the advent of appropriate enabling technology, high-voltage power lines now operating at 765 kilovolts (kV) might be able to operate safely and economically in the higher ranges of 1100 to 1500 kV, cutting losses by 50 to 75 percent, respectively.

In 1974 Seed Money researchers laid the scientific foundation for the development of several key advancements in such technology. Their work focused in particular on improvements in insulating materials, known technically as dielectrics, which would be required to handle the higher voltages.

High-voltage devices such as switches, connections, and transmission lines are protected from electrical short-circuiting by wide gaps between the so-called "hot" side of the circuit and the ground. Under ideal conditions, this gap would be filled with a perfect insulator, keeping the two sides safely separated, while simultaneously minimizing space and cost.

More typically, however, a safe device is large, cumbersome, and costly. The gap is usually filled with certain liquid dielectrics, such as oil, or as is often the case in high-voltage devices, the gap is made wider and filled with ordinary air or other gases known to have special insulating properties.

Unfortunately, under the stress of strong electric fields, which become stronger with higher voltages, the insulating properties of gas dielectrics break down. For a brief moment, the gas becomes a conductor of electricity, rather than an insulator, allowing the high-voltage current to jump across the gap with disastrous results.

Seed Money researchers were aware that certain gases were more resistant to "breakdown" than others and set out to investigate the underlying causes. The research examined the effects of strong electric fields on the behavior of gases at the atomic and molecular levels.

In particular, the work focused on the delicate balance between the rates of production and absorption (elimination) of a special class of electrically charged particles, called "free electrons." These particles exist naturally in minute amounts in every gas and, if concentrated in sufficient number, can carry a large electric current.

The researchers hypothesized that breakdown occurred when this balance tipped too far in favor of production. This would result in a nearly instantaneous population explosion of free electrons, which would be followed immediately by a large, violent electrical discharge.

Accordingly, they searched for a means by which certain electron manipulating properties could be introduced into gas dielectrics so that the balance would be tipped the other way. They looked for two properties in particular, one that promotes absorption, which eliminates free electrons best when they move relatively slowly, and another complementary property that promotes scattering, which works best on the faster free electrons and slows them down.

In this line of research, they were highly successful. Gases were identified that possessed the desired properties, and optimal mixtures were formulated that both improved insulation performance and lowered costs.

Further, in the course of the investigation, the Seed Money researchers discovered that toxic chemicals could be produced by sparks in the most commonly used gas dielectric, sulfur hexaflouride. This finding alone revamped industry work and safety procedures and greatly reduced previously unknown, but nevertheless prevalent, occupational risks.

Importantly for the future, this research contributed significantly to our understanding of how gases, when subjected to high electric fields, either resist or conduct high-voltage current. Understanding this behavior is of great importance to other advanced technologies, such as those which require extremely fast and durable high-voltage switching devices. These include high power lasers and particle beam accelerators, both of which are currently the subject of active research interest. They also include certain schemes for obtaining a virtually inexhaustible supply of power from a nuclear process that mimics the sun, called fusion energy.

Altogether, this Seed Money accomplishment generated considerable interest in the high-voltage equipment industry. It was the subject of several well attended international conferences and the focus of much follow-on work funded by private sector manufacturers and research institutes.

Perhaps more significantly, basic research into the fundamental behavior of materials under conditions of an imposed electric field led to increased understanding of how this behavior could be adapted to practical application. This knowledge not only led to the development of new and improved techniques for the safe and efficient handling of high-voltage current, but also opened new vistas of potentially important developments in advanced energy production and defense technologies.

New Tools for Science

Microcalorimeter

Some of nature's most intriguing scientific mysteries often lie just beyond our grasp because we cannot measure properly. Recently, however, Seed Money researchers developed a new, highly sensitive heat measuring instrument, called a microcalorimeter, which has begun to shed light on these mysteries and provide the means by which their underlying processes may be revealed.

Take for example the origin of man's most valuable mineral deposits, including those of iron, manganese, copper, zinc, silver, and gold. It is now believed that these deposits, mined on land near the surface, were once formed at great depths on the ocean floor near volcano-like hot springs, or so-called ocean thermal vents. A better understanding of how these mineral deposits were formed may lead to significant advances in our ability to locate and mine new deposits.

Unraveling this and other mysteries requires, in part, a basic understanding of the behavior of dissolved minerals in sea water at extreme temperatures and pressures. Yet, the underlying thermodynamic properties of mineral laden solutions in such regimes, cannot simply be extended from current data or more common experiences. Even normally stable properties are known to vary widely under such conditions and, until recently, could not be measured for lack of a reliable instrument.

In 1978 researchers funded by the Seed Money program embarked upon an uncertain path toward the development of such an instrument. The goal was nothing less than a device capable of the complete characterization of the most important thermodynamic properties, at temperatures up to 900°F and pressures up to 700 atmospheres, for a full range of solutions, including highly corrosive ones, such as strong acids and bases.

Their work made use of the fact that under special circumstances, if one could measure very precisely the faint amount of heat (energy) either given off or absorbed by a mixing reaction involving two highly dilute solutions or liquids, then everything else would fall into place. The special circumstances required, as a minimum: exact knowledge of the temperature, pressure, chemical composition, and amounts of the two liquids to be mixed; a carefully controlled mixing process to ensure completeness of the reaction; total absence of any gas or vapor phase in order to simplify the equations and eliminate extra variables; and a means of correcting for any outside influences that might adversely affect the data during the experiments.

If these conditions could be achieved under exacting standards, then the so-called "heats of dilution" could be measured precisely. This information, combined with other existing data, the well known laws of thermodynamics, and the equations of physical chemistry, could then enable the researchers to derive the remaining thermodynamic properties of the solutions in question.

The technical challenge was essentially one of building a device that could both withstand the extreme corrosiveness, temperatures, and pressures of the solutions envisioned, while simultaneously achieving levels of precision in measurement never before attempted. At the time, it was considered a high risk venture.

Within a year, the Seed Money researchers had built their device and demonstrated its powerful capabilities. They were enormously successful. Their device had circumvented a number of longstanding technical difficulties and produced results with high accuracies in previously unexplored regimes.

Moreover, the device was efficient and economical. Because of its simplicity, many tests could be run per day, heralding the collapse into months of what otherwise would have taken years of difficult and expensive research using different approaches toward the same end. The device gained immediate acceptance within the established community of basic chemistry research and became a mainstay of a continuing and highly productive line of work in high temperature and corrosive environments.

Today, the thermodynamic properties of solutions at high temperatures and pressures have many uses. Not only are they being used by geoscientists in unravelling the mysteries of mineral formations, but they have many other practical applications. They are necessary in understanding fluids used to extract energy from the earth in geothermal technologies. They are important in designing a properly protected means for permanently disposing of high-level radioactive waste. They are helping power engineers design better steam generators that are more resistant to corrosion and cracking. They are fundamental to research work in electrochemistry aimed at the development of new electrolites used in advanced batteries and fuel cells.

The successful development of the microcalorimeter was a significant advance. It has since assumed a principal role in major investigations of thermodynamic properties and has proven to be an indispensible tool for basic research. Developed modestly with no stated application, it now serves in many diverse and important ways never envisioned.

Positron Probe

A unique and potentially powerful tool for studying atoms, their orbiting electrons, and the important physical details of the surfaces of materials, recently took a significant step forward with the aid of Seed Money research.

This tool, which makes use of a rare subatomic particle known as positron, can be used to probe the atomic building blocks of nature in ways that no other tool can. Its application promises new insights into economically important areas of scientific endeavor as diverse as physical chemistry, behavior of materials, and microelectronics.

The power of this new tool stems from the unique properties of the positron. This particle is relatively lightweight and carries a positive electrical charge, enabling it to be easily manipulated by an electric field. It can be accelerated and precisely controlled at varying intensities, focused with accuracy, stored briefly, and garnered with others in sufficient numbers to be pulsed onto surfaces like a bright light beam.

Similar in many respects to its sister particle, the electron, a beam of these particles may be used to make the positron version of the more familiar electron microscope. Because the positron carries a charge opposite to that of the electron, and is thus attracted to electrons orbiting at the surfaces of atoms instead of being repelled, such a microscope would give scientists valuable new perspectives and potentially sharper resolution of certain structural details.

More significantly, however, is the fact that the positron tends to annihilate itself in the presence of an electron. In the process, it also destroys the electron and broadcasts a final, information-laden message about the precise location and circumstances of its destruction. This message also contains many scientifically important physical details about the positron's hapless electron partner.

It is this ability to search out specific parts of an atom's structure, namely the outermost orbiting electrons, or alternatively concentrations of electrons in the surface structures of materials caused by defects or the presence of impurities, and to send back physical data about these conditions that offers so much potential for scientific investigation.

Why are these particular electrons so important? Virtually all natural phenomena observable in everyday life are governed by the ways in which the specific arrangements of electrons in the outermost shells or orbits of atoms interact. The physical characteristics of these arrangements, such as the size of the shells, the number of electrons, and how tightly they are bound, establish the laws of chemistry; prescribe how individual atoms form into solids, liquids, and gases; and dictate how different elements combine into substances ranging from solid mixtures and metal alloys to liquid solutions and complex molecules.

Importantly for many high-tech industries, these electrons also impart to substances many of their unique properties, such as strength and ductility, electrical conductivity, resistance to corrosion, and in certain instances, how their molecular surfaces bond with others. Hence, a fundamental understanding of the physics of an atom's outermost electrons and the composition of materials at the atomic level lies at the heart of many crucially important technological advances.

In the highly competitive aerospace industry, for example, there is a continuing and pressing need for stronger and lighter structural materials. In recent years, this need has been met in some instances with a new class of materials, called epoxy-based, carbon-fiber composites. Positron research is now being used to investigate the molecular bonding characteristics of various types of composite fabrications. The study of damaged sections from military jet aircraft, using positron probes, has given rise to new theories as to why certain fabrications seem to be much stronger than others.

Similarly, the search for why some very strong metals are made impractical because of their brittleness has led to the study of atomic structures on the surfaces of the microscopic crystals which form the metals. It is at these surfaces, called grain boundaries, where slippage occurs, causing a material to be brittle and break under stress. A study of the migration and position of certain impurities at these surfaces, aided in part by positron diagnostics, has led to a process which increases adhesion at the grain boundaries and resulted in the "ductilization" of previously useless, super strong but brittle alloys (see Nickel Aluminide). Other such applications of positron research abound, and progress in the field is gaining momentum.

Earlier, however, there had always been two major problems confronting positron researchers, both of which research funded by the Seed Money program helped to solve. First, in most practical applications (other than those requiring ultra-high vacuums) one could never get reliably enough positions for a useful diagnostic. Positrons are very rare; they live on the average of only one billionth of a second. Second, when one did get them, they were either too fast or of such widely varying energies that the resulting signals were nearly impossible to interpret meaningfully. What was needed was a reliable means of producing an abundant source of slow and relatively monoenergetic positrons in environments other than ultra-high vacuums.

In 1978 and 1979, researchers funded by Seed Money set out to solve these problems with a two-pronged attack. First, they investigated a number of different sources, particularly those known to be prolific and energetic positron emitters. This necessitated a containment system for safety and required the positrons to pass through a protective window, a process that would ordinarily diminish the resulting beam's strength. Ultimately, they found a window that was relatively transparent to fast positrons and devised a safe means of producing an intense beam.

Simultaneously, they explored a variety of materials that might be used to slow down, or moderate, fast positrons without consuming too many of them in the process. Ultimately, an efficient moderator was found to be tungsten. In addition, the researchers developed a heat treatment method for the tungsten that removed oxides and greatly reduced the concentration of surface defects, such as holes between molecules or atoms, which limited the number of slow positrons reemitted. As a result, the researchers were able to devise a reliable means of producing a beam of slow, monoenergetic positrons about the diameter of a pencil flowing at the rate of 100,000 positrons per second.

Although copper moderators developed elsewhere were known to be of higher efficiency, they had to be used under ultra-high vacuum conditions to prevent loss of efficiency due to rapid contamination and oxidation. The Seed Money tungsten moderator, by contrast, did not significantly oxidize when exposed to air. This attribute, aside from improving ease of use, also permitted its broader application to such areas as electron scattering in gases. A description of how electrons behave in gases is important in areas such as plasma physics, laser technology, and the chemistry of the upper atmosphere.

These breakthroughs proved to be significant steps in the further development of practical diagnostic tools, particularly in the area of analytical chemistry. It elevated positron research to a new and highly productive plane.

Shortly thereafter, using the Seed Money tungsten moderator, researchers at Brandeis University successfully performed the first laboratory demonstration of low energy positron diffraction, another useful surface analysis technique. This technique complements and may even surpass in overall utility and ease of use other more well-established methods.

Today, positron researchers around the world are investigating problems in many diverse areas, including annealing, wear, and fatigue in metals and alloys. Positrons are also being used to investigate the chemical properties of gases, solutions, and even such biological molecules as membrane proteins and enzymes. Many of these researchers are using tungsten moderators, or improvements thereon, which were originally researched by the Seed Money program.

The success of this research made a measurable contribution to a larger body of work and helped make positron spectroscopy more of a practical reality, with broadened applications.

Atom Science

Once in a while in the field of scientific instrumentation, there comes a device of such increased power and versatility that an entire spectrum of research based on traditional methods of measurement is revolutionized. Such is the story of a new and extraordinarily precise measuring technique, called resonance ionization spectroscopy (RIS). The origin of its development may be traced to three Seed Money projects funded in 1975, 1978, and 1982.

The power of this technique lies in its remarkable capability to search out, detect, count, and, if desired, extract for further use, a single atom of a specified type among literally billions of billions of atoms of any and all other types. In an analogy to an old saying, it's like finding a needle in a haystack; except with the RIS technique one has the added benefit (important to scientific research) of knowing that all the needles have been found and accounted for. Compared to previous techniques, RIS can improve the sensitivity of atom counting by an astonishing six orders of magnitude, or a million-fold.

Counting individual atoms, particularly those in rare amounts or unusual forms, is crucially important to many fields of fundamental research. It is also vital to commercial research and development in many burgeoning and competitive high-technology industries.

In the miniaturization of computers, for example, wherein a million transistors may be placed on a single silicon chip the size of a dime, the wires carrying the electrical signals have become so narrow (10 to 100 atoms wide) that the presence of a single atom of an unwanted material, such as iron, can disrupt reliable performance. Hence, as a means of improving their products and manufacturing processes, makers of such devices are keenly interested in scientific instruments that can detect and characterize impurities on this most fundamental of scales.

Counting atoms is also important to the study of geology, minerals science, hydrology and natural history. Predictive models of slowly migrating water in underground aquifers, for example, may be validated by age dating techniques that rely on measuring minute amounts of a noble gas (krypton). The same is true for understanding the earth's long term climate cycles, as evidenced by the same noble gas trapped in deep cores of permanently frozen antarctic ice. In both cases, not only must the gases be identified and isolated, but individual subdivisions (isotopes) within their own atomic species must be sorted out and counted precisely.

In the climate cycles research, standard techniques require as much as one thousand tons of antarctic ice to determine a single data point in time. With the RIS technique, a pound or two may now suffice. Similarly, the Shroud of Turin, believed to be the burial cloth of Christ, has never been scientifically dated because previously existing dating techniques would have damaged or destroyed an unacceptable amount of material. Hence, with the advent of RIS, size dependent constraints such as these may vanish altogether.

In another class of applications, RIS affords new opportunities to search for rare events of great interest. Such events, if they could be detected reliably, might confirm certain theories about the processes of the sun, which involve the measurement of solar neutrinos. Or, they may lend support to the grand unification theory of the basic forces of nature, a clue to which may be gleaned from observing the so-called process of a "double beta" decay.

In both cases, experiments involve the detection and monitoring of extremely rare events. In a proposed solar neutrino experiment, for example, only 100 atoms of krypton-81 are expected to be produced in a tank containing 100,000 gallons of ethylene bromine over a period of 6 months, each one of which needs to be detected.

The RIS technique of detecting, sorting, and counting such small amounts of highly specified atoms is an extraordinary technological feat. In reality, the machines that perform the work constitute a unique configuration of some of the very latest advances in laboratory equipment and scientific instrumentation.

Today, an experiment making full use of RIS capabilities is likely to employ a large complement of hardware. This could include ultraclean containment vessels, powerful vacuum pumps (which for cleanliness purposes use no oil whatsoever), highly sensitive counters; and signal amplifiers. It might also include electromagnetic devices that filter out unwanted particles; cryogenic probes that "bunch" atoms together via condensation at temperatures of only a few degrees above absolute zero; other devices that manipulate atoms to strike a receiving plate, implanting them for temporary storage (see Ion Implantation); and still others that release them upon demand for further analysis (see Laser Annealing).

The ingenious exploitation of all these capabilities and their assembly into a compact and efficient instrument was the successful outcome of the 1978 and 1982 Seed Money projects. The 1978 project applied the RIS technique and much of the above hardware to the study of surfaces of solids. The 1982 project focused on the measurement of rare atoms in the medium of gas. Both broke new ground.

It was the 1975 Seed Money project, however, in which the heart of the RIS technique was developed. This involved the use of lasers in combination with a developing field of science called photophysics. Lasers are electrically powered devices that emit intense beams of highly coherent and finely controlled light. Photophysics is the study of how light interacts with matter and, in particular, with the atoms of matter and their orbiting subatomic particles, called electrons.

An example of how light and matter interact may be recalled by what happens to ordinary table salt when it is tossed into a flame. A rainbow of colors is immediately given off. The colored light arises from the heat of the flame, which causes certain electrons in the atoms of the salt to become momentarily excited. This increases their energy and lifts them temporarily into higher but unstable orbits, called excited energy states.

After a brief moment, they collapse back to their lower and more normal orbits, called ground states. During the downward transition, however, the extra energy of the excited state is released to the environment, and seen by the human eye as a perfectly pure emission of colored light.

As it happens, the color of the light is like a fingerprint or signature. Each color may be uniquely associated with each type of electron transition for each type of atom.

In 1975 Seed Money researchers hypothesized that, with the advent of tunable lasers, they might be able to reverse this process and use it to their advantage. That is, they would try to tune laser light to the exact color recognized only by the selected electron transition associated with the atom of interest.

Using the laser, they proposed to pump in just enough light energy to hit the right electron and lift it up to a preselected excited state, wherein it is more loosely bound to the atom's nucleus than when it is in the ground state. Then, while the electron was vulnerable, they would hit it again to remove the electron altogether. If they could remove the electron, which is negatively charged, the remaining part of the atom would become a positively charged "ion," which could then be drawn to a negatively charged plate, detected and counted.

Thus, they sought to design a two-step process. The first step was highly selective, intended to search out only the one type of atom of interest and begin the process toward electron removal. The second step was to remove the electron in a process called ionization.

The total process is called "resonance ionization" because it works only when the laser light is perfectly tuned in harmonic resonance with the amount of energy required by the selected electron transition. Further, because the light passes invisibly by all other species of atoms and their electrons, this technique provides an extraordinary degree of selectivity.

While the concept of resonance ionization was well established before the Seed Money research and, in fact, had been demonstrated earlier on atoms of helium, the technique was not practical because it required the use of extremely powerful lasers. Further, it was highly skewed. In the case of helium, for example, only one-tenth of one percent of the total energy required for the two step process went into the all important first step. The remainder went into the ionization step.

The thrust of the 1975 Seed Money project was to explore ways to make RIS more practical. They hoped to use a commercially available, low power laser to accomplish selectively the first step, followed by some other technique to complete the second.

For purposes of study, they decided to pick one of the easiest elements in the Periodic Table to ionize, cesium (helium is the most difficult), on which their proposed techniques were most likely to succeed. They tried several ionization schemes, including the use of electromagnetic fields and collisions with other gas molecules under pressure. Both worked. They established for the first time the feasibility of one-atom counting.

As is often the case in basic research, however, the real breakthrough was more subtle and unexpected. In the process of working out their theories and setting the procedures for their experiments, they learned a great deal about photophysics. Using this new knowledge, they came up with a number of schemes whereby low power lasers could be used to achieve *all* the steps necessary, without resorting to other and more cumbersome techniques.

Since then, RIS schemes using low power lasers have been developed for all elements in the Periodic Table except two, helium and neon. These elements still require lasers of a type not yet commonly available. Importantly, with subsequent refinements to RIS, accomplished by the 1978 and 1982 Seed Money projects, nearly every atomic species of scientific or commercial interest, from gaseous to solid form, can now be investigated with an unprecedented degree of selectivity and precision.

In response to intense interest on the part of potential users, a commercial firm was established to develop and manufacture RIS instruments and provide related advisory services. RIS won two IR-100 Awards from *Research & Development* magazine and is the subject of a number of United States patents.

The RIS technique has so profoundly altered the field of atom science that literally hundreds and perhaps thousands of researchers across a multitude of disciplines are now conducting or contemplating experiments not possible a decade ago. The new knowledge produced as a result will undoubtably be equally impressive.

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