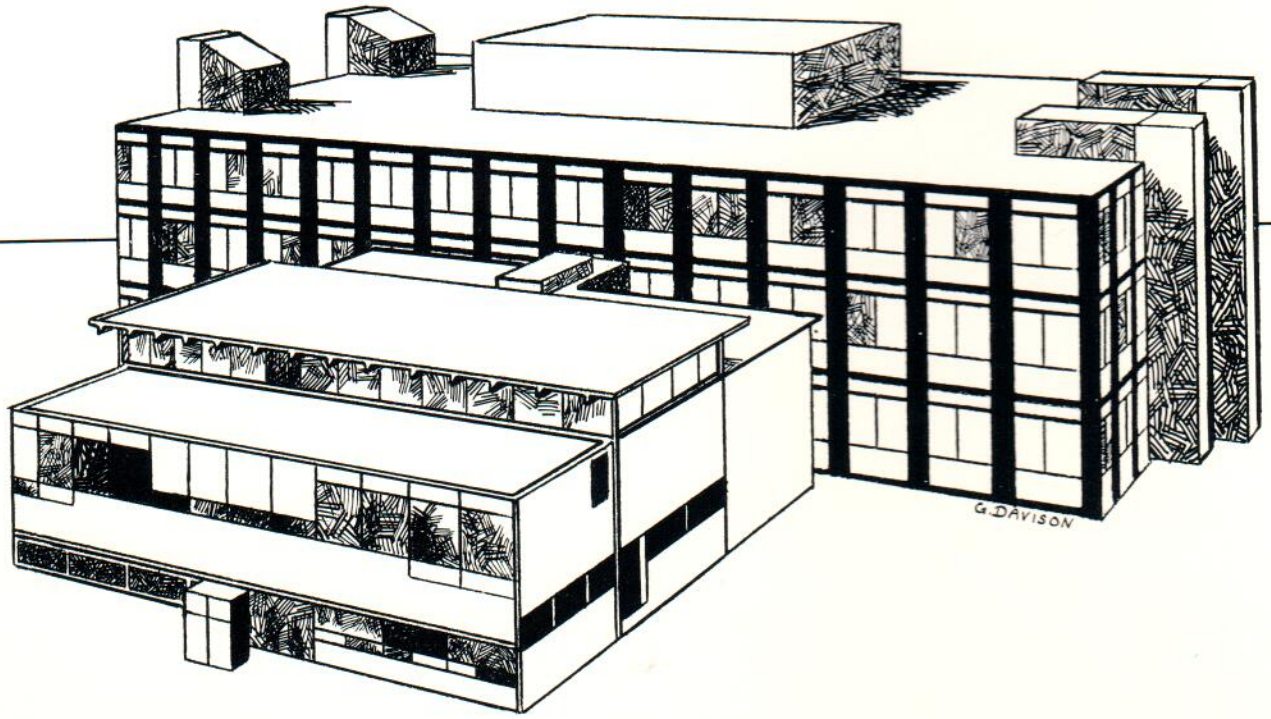
BOSTON
BIOMEDICAL
RESEARCH
INSTITUTE

Annual Report 1980

BOSTON BIOMEDICAL RESEARCH INSTITUTE 20 STANIFORD STREET, BOSTON, MASSACHUSETTS 02114



"You're searching, Joe, for things that don't exist; I mean beginnings. Ends and beginnings—there are no such things. There are only middles."

Robert Frost

REPORT OF THE EXECUTIVE DIRECTOR

Peter F. Davison, Ph.D.

This year the staff of the Institute can look back on a decade of difficulties overcome, challenges met, and a growing strength. The steady progress of basic research continues—only noted by the public when a development hits the headlines: recombinant DNA, brain peptides, hybridomas. It is ironic that the decade which has seen Wall Street's sudden infatuation with basic research in medicine has also seen a wavering of federal support for it. Fortunately, small groups of scientists and supporters, including our trustees, testified or wrote repeatedly to secure from Congress some assurance that the research enterprise, emaciated though it is, will not be allowed to die. We are assured that 5000 new or renewed grants will be funded each year. Congressional appropriations have not kept pace with inflation, however, so the vigor of research in the United States is waning. The decline of the U.S. predominance at international meetings and in the scientific literature over the decade is obvious. The nationality of each new discoverer is, of course, not important; science advances on an international front. A glance about will show the technological advances of the decade that are part of everyday life. Solid state electronics, for instance, is everywhere—from calculators to cameras to pacemakers. Scientific progress brings economic progress which we need; and we need improved diagnostic and therapeutic techniques. They are not a luxury but a necessity. The demand for health care cannot be allowed to escalate beyond its present 10% of the gross national product without threatening our economic balance.

So, there is the challenge! Where does the Institute stand? The year 1980 sees BBRI firmly established with many vigorous research programs and substantial grant support as the figures on page 15 show. But I am sometimes asked, what are the actual *products* from the millions of dollars BBRI has received from federal and voluntary agencies and from our generous supporters in the private sector? I can point to some commercial or near commercial developments which will aid treatment or diagnosis of some patients, but the fruition of any one project into a saleable and useful product or technique is quite unpredictable. Our real products are new knowledge, described in congresses or written in books, pamphlets, journals; and ideas, generated, passed on, provoked. Is research really that valuable? Ask Wall Street.

The potential importance of genetic engineering, for instance, has been widely recognized by investors, but who started it? Looking back, it is obvious that recombinant DNA technology began when investigators probed the mechanism of genetic recombination in simple bacteria. Their experiments presumed the double helix of DNA; that discovery depended upon the isolation of pure DNA, and that study began with Miescher's curiosity about the viscous mess of pus in the bandages of soldiers wounded in the Franco-Prussian War. So who is responsible for this or that discovery? Rarely is one individual uniquely responsible; all stand on the shoulders of the giants before them to see further and clearer. We cannot predict which research programs briefly described in this report will stimulate future investors or investigators, but that is one reason that biological science is so exciting. Work on an amoeba may illuminate function in a dividing, fertilized egg or the contraction of muscle, and studies on a blowfly may increase our understanding of kidney function. Any avenue of basic research on the constituents operating in the living cell has implications for other approaches, other cells, and other animals. A real strength in a small institute like BBRI is the frequent interaction and communication between investigators.

What can we foresee in the next decade? With the changes of Administration, policies will change. We hope that many of the regulatory impediments to research will be lessened, but certainly our need for help from our corporation members and friends will not decrease. I thank them all on behalf of the staff and ask their continued interest and support while the staff does its job, working toward an understanding of—then an improvement in—man's condition.

REPORT OF THE PRESIDENT

John A. Shane

During fiscal 1980, the trustees of Boston Biomedical Research Institute implemented several significant programs designed to increase awareness and understanding of BBRI's objectives and accomplishments among its trustees, corporation members, and friends.

The scope of the Development Office was expanded and Penelope W. Stohn was elected its first full time officer. Under her leadership the layout, contents, and frequency of *News from the Institute* were improved; a piano concert was sponsored by BBRI in the spring; a series of free lectures by distinguished scientists examining the future of medical science was scheduled; and this form of the Institute's Annual Report was designed. Through these activities and others, BBRI has become known to a larger circle of friends than ever before.

The importance of maintaining the high quality of BBRI's work through the recruitment, retention, and advancement of an outstanding research staff was reaffirmed by the trustees, and steps were intiated to ensure that this vital process receives continuing attention.

A staff committee, chaired by Dr. Henry Paulus, prepared a statement of BBRI's goals for the next five years, including projected needs and requirements for staff, space and research facilities, and funding. This comprehensive report provides a solid basis from which possible future courses of action can be evaluated and selected.

A Development Committee comprised of trustees and corporation members under the chairmanship of Eustis Walcott, Jr., Vice President, was formed. This Committee will not only examine the Institute's annual financial requirements, but also recommend ways to meet BBRI's long term goals and needs. The Development Committee meets monthly with officers and staff of BBRI and serves as an excellent communications link between the various constituencies of the Institute.

Closely coupled with the public's traditional interest in advances in medical science is a deep concern regarding the possible hazards or risks associated with some of the processes and products of medical research. BBRI has always maintained rigorous safety standards and procedures meeting or exceeding stringent federal regulations concerning medical research practices. Nevertheless, to ensure that the trustees are aware of any changes in regulations or procedures, the Biosafety Committee of BBRI was expanded to include a trustee representative. Vice President John B. French, an attorney, was elected to serve in that position.

I regret to report that Abraham Winer, a corporator of BBRI since 1968, died in December 1979. Scott Ricketson, a corporation member since 1977 and H. Shippen Goodhue, a Vice President and trustee of BBRI for over 10 years, have chosen not to stand for reelection in 1981. I am pleased that Mr. Goodhue has agreed to remain a corporation member.

The excellent quality of the Institute's work can be partly attributed to the staff's continual insistence that it strive to improve its already high standards of performance. I believe that this commitment is shared by BBRI's trustees and corporation members, and I am grateful to them for their support, encouragement, and considerable participation in the affairs of the Institute during the past year.

DEVELOPMENT AND AGING

To study the complex processes of development and aging BBRI scientists use a great diversity of model systems including mouse embryos, tissues and tissue cultures, roundworms and even a simple microorganism.

"At first the infant, mewling and puking in the nurse's arms," . . . . and then "second childishness and more oblivion, sans teeth, sans eyes, sans taste, sans everything."

– Shakespeare

Collagen—The Glue That Holds Us Together

Collagen, the predominant protein in the body, provides the strength of tendons, cartilage and skin, braces the joints, anchors the teeth, and aids in the closing of wounds. The strength of collagen fibers depends upon the formation of chemical bonds between the protein molecules. There are several types of collagen, and during growth the types in one tissue may change. Although neither the function of each type nor the control of their synthesis is well understood, it has been established that many diseases result from abnormalities in collagen distribution and the building of chemical bonds. Drs. P. Davison, M. Brennan, and R. Lee are investigating the growth and developmental changes in the collagen-rich tissues of the eye. Because collagen fibrils cannot stretch, they must be constantly broken down and rebuilt in a growing eye. These studies have direct relevance to several abnormalities of disease conditions of the eye and are also adding basic information vital to understanding growth, wound repair, diseases of the joints and skin, and perhaps aging.

Cleft Palate

Cleft palate, one of the most common malformations seen in man, has been the subject of extensive research. The developmental events which generate this birth defect, however, have not been firmly established. Dr. B. Jacobson has focused on the possible mechanism by which cortisone delays movement of two embryonic structures which normally grow and fuse to form the roof of the mouth. Experiments with mouse embryos show that cleft palate may result from cortisone-induced changes in the synthesis of a key intercellular compound, hyaluronic acid in palatal tissue. After cortisone treatment, mouse strains susceptible to cleft palate show a drop in the level of hyaluronic acid. Dr. Jacobson suspects that swelling by the accumulation and hydration of hyaluronic acid in the tissue is at least partially responsible for normal development of the palate.

Tissue Culture of Aged Cells

In their current research on the biochemistry of aging, Drs. R. Burrows and P. Davison compare mechanisms by which young and old animals adapt to changes in their enviroment. The ability to regulate the metabolism of protein is one such mechanism. These investigators are now studying two aspects of protein metabolism: the capacity of cells to control the rate of protein degradation and to change the concentration of special proteins in response to nutritional and hormonal stimuli. The latter changes are known to be slower in older animals. Experiments with cultures of liver cells from mice of various ages allow the behavior of the cells to be observed under well-defined experimental conditions. These cells provide a convenient experimental system for the examination of some aspects of the aging process at the molecular level.

Worms— Genes, Nutrition, And Aging

Because aging rates are inherited characteristics, they must somehow be controlled by the genes. In order to investigate how genes control aging rate, Dr. D. Mitchell is trying to isolate organisms with altered (mutated) genes that result in altered aging rates. He uses a small roundworm that ages 1,000 times faster than humans as a model aging system. This short lifespan allows genetic and nutritional experiments that would take years in humans to be done in a few days or weeks. For example, normal roundworms grown with bacteria live about 23 days. Worms placed in a rich chemical broth at hatching, however, develop very slowly, and then age slowly. These worms live from 65 to 70 days— more than twice the normal lifespan. A variant worm strain has been isolated that grows rapidly in the chemical broth and that lives about 25 to 30 days. Genetic crosses between the strains are in progress. These crosses and additional nutritional experiments will lead to a better understanding of how genes and environment help regulate the rate of aging.

Computer Analysis of Development and Aging

To have a rational basis for slowing the aging process, we must understand the mechanisms involved. Higher organisms are so complicated that the multiple causes underlying aging are difficult to recognize and analyze. Comparative biochemistry has taught us that mechanisms uncovered in simple organisms will in all likelihood apply to more complex ones. Hence, Dr. B. Wright and her colleagues are involved in an in-depth analysis of development and aging in *Dictyostelium*, a simple (microbial) model system with only two cell types. The analysis of *Dictyostelium* metabolism has uncovered so much information and complexity that a computer model has become necessary for a realistic integration and interpretation of the data. The fact that many of the computer-based predictions have been substantiated experimentally encourages these investigators to pursue their novel approach.

METABOLISM AND ITS REGULATION

Research at BBRI is concerned with many types of regulatory mechanisms, ranging from control of activity of the enzymes that catalyze metabolic reactions, to control of the distribution of substances within cells as well as between cells and their environment. These studies provide basic insights into the processes of growth and development as well as into possible defects that may lead to degenerative changes and disease.

Enzymes

Enzymes are the biological catalysts that make possible the thousands of chemical reactions occurring in the living cell. Enzymes, however, do not simply catalyze reactions—they are designed to be regulated so that catalysis occurs only when it is needed by the cell. The study of enzyme regulation will thus provide important insights into cellular metabolism. Dr. H. Paulus and his associates are studying the control of various enzymes in order to learn more about the mechanisms which integrate biosynthesis processes essential for growth. Another aim of this research is to discover abnormal conditions that may be caused by aberrations in enzyme regulation. Small changes in enzyme structure, caused either by environmental or genetic factors, can lead to major metabolic disturbances. Experiments are now in progress to determine whether alterations in the regulatory properties of certain enzymes may be responsible for some of the degenerative changes that accompany the aging process in man.

Energy Production

Several mechanisms regulate enzyme activity in the cell. One mechanism which has been difficult to approach experimentally is the control of this activity through the spatial distribution of enzymes in the cell. In studies of two enzymes necessary for the synthesis of a carbohydrate called trehalose, Dr. K. Killick concluded that they could carry out their function only if located very close to each other. To mimic this situation in the test tube, Dr. Killick is attaching the enzymes to a surface in order to study the effect of their proximity on their concerted activity. These results will be compared to predictions made with the help of a computer model of this system.

Control of Enzyme Activity By Compartmentation

Energy for cellular needs is derived from the combustion of food materials through a series of chemical reactions ending in the production of ATP. As mentioned above, this process occurs within microscopic compartments, the mitochondria. Drs. D. Sanadi, S. Joshi, J. Hughes, and R. Houghton have identified one of the key proteins, coupling factor B, in the reaction sequence leading to ATP production. Mitochondria from which factor B has been removed can no longer use food material to drive ATP synthesis; the gears that are driven by combustion disengage from the gears that drive ATP formation, and the cellular machine idles. When factor B is added back the gears become engaged, and ATP production starts. The role of factor B as a biological regulator of ATP production may have implications for such disorders as obesity, hyperthermia, and adaption to cold stress.

Transport

In living systems, membranes form barriers around cells and compartments within them. The movement of chemicals across membranes, referred to as transport, plays an important role in the regulation of biological processes. The transport of phosphate and of calcium is studied in detail at BBRI.

Phosphate is central to the energy metabolism of all cells. Cells store energy in the form of adenosine triphosphate (ATP), which is cleaved to produce a phosphate ion when the cell uses energy. Phosphate has to be transported into the cellular compartment, the mitochondrion, to make regeneration of ATP possible. Dr. H. Wohlrab and his associates have isolated from the mitochondrial membrane the protein responsible for phosphate transport. They are attempting to identify its molecular structure and function. Their studies may help to identify defects of transport proteins that may occur in senescence and in various diseases.

Calcium is a key element in the control of muscle contraction. Drs. N. Ikemoto, C. Hidalgo, M. Rosemblatt, and T. Scott are studying calcium transport across a membrane known as sarcoplasmic reticulum. The importance of calcium lies in the fact that its combination with certain proteins in the contractile apparatus, the so-called regulatory system, leads to the contraction of muscle. Extensive studies by Drs. P. Leavis, S. Lehrer, J. Seidel, T. Tao, J. Gergely and their colleagues have characterized this system by using probes sensitive to light and magnetic fields.

Studies by Dr. Seidel on the smooth muscle found in the walls of blood vessels deal with a different type of regulation which involves a combination of muscle proteins with phosphate—a process which in turn is also controlled by calcium. These investigations on smooth muscle may lead to a better understanding of the abnormalities involved in diseases such as arteriosclerosis and high blood pressure.

MUSCLE

Muscles move our bodies; the heart muscle pumps the blood. Muscle tissue is a key component of blood vessels and various hollow organs such as stomach, intestines, and uterus. The study of muscle function and structure is essential for understanding how these systems work in the normal organism and provides a basis for dealing with diseases such as muscular dystrophy, heart disease, and hypertension.

Mechanism of Muscle Contraction

The understanding of muscle contraction in health and disease depends on the detailed knowledge of cellular components involved in movement or force generation—the contractile machinery. They include the proteins myosin and actin, which form rods about one ten thousandth of an inch long and one millionth of an inch in diameter. Muscle contraction fueled by ATP depends on the sliding of these two kinds of rods past each other. BBRI scientists are studying the process that provides the driving force. The minute details of the chemical structure of the proteins involved are studied by Dr. R. Lu. Crucial movements among and within the proteins are being characterized by Drs. P. Leavis, S. Lehrer, J. Seidel, T. Tao, and J. Gergely, who have attached chemical groups to the protein in selected positions. These probes fluoresce upon being irradiated with light or respond to magnetic fields. Finding the blueprint for the normal working of muscle will make it possible to understand various diseases that involve muscle tissue.

Development, Adaptation, and Transformation of Muscle Tissue

A given muscle in the adult contains a set of proteins appropriate to its function. This is the result of a complex developmental process, since in the embryo the protein composition of the muscles is quite different. All genes (which control protein synthesis) are present from the earliest embryonic time through adult life. Therefore, the question arises how genes that code for various proteins at different stages of development become active. BBRI scientists study several aspects of this problem. Dr. S. Sarkar and his colleagues are concerned with the processes that control the transcription of genes into the so-called messenger RNAs, and the translation of these into proteins. Complexes of messenger-RNA with a well-defined set of proteins form particles whose properties and metabolism may give clues to the regulation of gene expression.

On another level, Drs. F. Sreter and J. Gergely and their colleagues are studying ways in which gene expression is altered by the connection between nerve and muscle function itself—for instance, stimulation of the intact nerve, immobilization of the muscle, or cutting of the nerve. The study of these processes will provide a better understanding of normal developmental and adaptive processes and may also give clues to processes that occur in muscle diseases and in aging.

Heart Hypertrophy

A particularly interesting instance of adaptation is the response of the heart muscle to an increased work load. Dr. F. Julian and his colleagues have been carrying out studies on heart enlargement, hypertrophy, produced by constricting the pulmonary artery. Since heart contains not only muscle cells, but also connective tissue cells and blood vessels, it is important to know to what extent the force-producing muscle cells grow in size in comparison to the other components. It is known that after a certain degree of increase in size, failure may occur. Failure may be due to the formation of functionally inferior molecules or to the collapse of other metabolic processes. Drs. F. Sreter and J. Gergely, in collaboration with Drs. Eugene Braunwald and Mark Pfeffer at the Peter Bent Brigham Hospital, have been studying cardiac responses in rats that spontaneously develop hypertension, a possible model of the human disease. In these animals there is clear indication of a shift in the type of contractile proteins present in heart muscle. The question arises whether this is an expression of a disease process or whether it is a beneficial adaptive response.

Studies on Human Muscle

Each muscle contains both fast and slow fibers, but their proportion differs depending on the functional requirements. Moreover, certain people have more of the fast fibers and others have more of the slow fibers, which makes the latter better suited for marathon running and the former more adept at the 100 yard dash. Recent advances have made it possible to study individual muscle cells or muscle fibers and establish the characteristic constellation of the various proteins found in a given fiber. Studies by Drs. F. Sreter, K. Mabuchi, J. Gergely and visiting scientists associated with them have shown that human muscle fibers contain different sets of protein molecules. The fact that this analysis can be carried out on minute amounts of material makes it possible to study diseased muscle protein composition in various diseases. This program not only helps in pinpointing defects that are associated with certain diseases, but may also provide a more accurate way of detecting individuals who are carriers in families where certain diseases are known to be present.

THERAPEUTICS, DIAGNOSTICS

In the course of fundamental studies, an investigator may see the possibility of pursuing a discovery that shows promise for early application to health care.

Malignant Hyperthermia

Malignant Hyperthermia is due to an inherited trait and is life-threatening when a susceptible individual is given a certain type of anesthetic, such as halothane, or engages in strenuous exercise. Drs. F. Sreter and K. Mabuchi are collaborating with Dr. John Ryan of Massachusetts General Hospital and Dr. Paul Allen of Peter Bent Brigham Hospital in a study of the basic mechanism underlying this condition in order to arrive at a simple and reliable means of detection. Studies on muscle biopsy samples show abnormalities in calcuim metabolism. Dr. Sreter and colleagues have developed a test and are currently screening patients scheduled for surgery to detect individuals at risk from halothane anesthesia. This work has led to further investigation of muscle fibers, and may lead to new techniques for understanding calcium metabolism. These studies may be of importance in the detection of other neuromuscular diseases.

Primary Biliary Cirrhosis (PBC)

PBC is a rare liver disease seen predominantly in women over thirty, and is difficult to distinguish from other chronic liver diseases. The blood of most PBC patients carries antibodies to mitochondria. The presence of these antibodies has served as one of the important diagnostic criteria for PBC, but the present method for detecting them is complex and difficult. Drs. S. Joshi and D. Sanadi have devised a simple method for detecting and measuring these antibodies in blood. Clinical use of this diagnostic test is being explored while further improvements in technique are being made. When the test becomes available, it may be possible to provide earlier treatment for PBC.

Antibiotics

The discovery of antibiotics and their therapeutic potential about 40 years ago has had a tremendous impact on the treatment of infectious diseases. The search for new antibiotics with improved characteristics is still actively pursued. Because it is not known why antibiotics are produced by certain microbes, the detection of new antibiotics must rely on inefficient random screening. Drs. H. Paulus and N. Sarkar have now discovered that the peptide antibiotics are produced by bacteria in order to control gene expression when the bacteria form spores. This suggests that new antibiotics will be found among spore-forming microbes and that the greatest antibiotic production will occur under the conditions which favor the formation of spores. More fundamentally, these studies reveal a striking analogy between the function of peptide antibiotics in bacteria and peptide hormones in animals and man. Studies on how these primative bacterial hormones regulate bacterial differentiation may contribute to our understanding of human endocrinological disorders and birth defects.

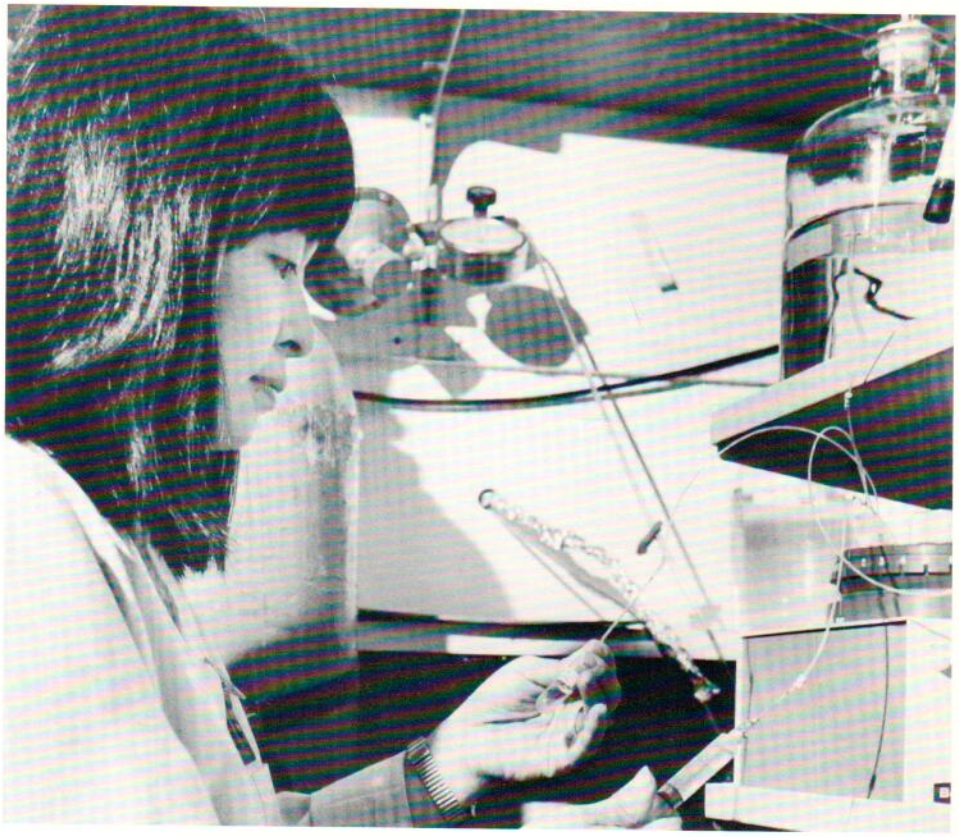
Nucleotides

Nucleic acids are long strands of macromolecules that can line up in double-stranded fashion. The double helix of DNA is the best-known example; the complementarity of the strands is the basis of faithful DNA replications and heredity itself. Seizing on this phenomenon, Drs. S. Srivastava and J. Benner in Dr. A. Nussbaum's laboratory are synthesizing artificial nucleic acids (oligonucleotides) which form double-stranded regions with natural nucleic acids (hybrids), thereby disturbing their normal structure and function. They are seeking the particular type of oligonucleotide most likely to cause such disturbances. These hybridizations are expected to generate points of weakness at specific locations in the DNA molecule. It then becomes possible to dissect DNA at desired sites—a technique of potential use in genetic engineering.

Yeast Infections

Candida albicans is a pathogenic fungus causing a variety of chronic, debilitating, and even life-threatening diseases in certain sensitive individuals. Antibiotics currently available are often ineffective against this fungus, or too toxic. *C albicans* has two different modes of growth, only one of which is thought to cause infections. Blocking the transformation to the invasive mode might constitute an effective therapy. The change from one mode to the other is a complex process, involving many biochemical reactions and pathways; some of these steps may be potential targets for therapeutic intervention. Dr. R. Emyanitoff has a broad research program to detail the metabolism and regulation of *C. albicans*. With the aid of computer modelling she hopes to identify steps critical to an effective treatment.

ENVIRONMENT



Cadmium

Cadmium is an industrial pollutant that is becoming an increasingly serious health problem. Toxic consequences of cadmium poisoning include cancer and serious bone disorders. In the early sixties, Dr. D. Sanadi discovered that cadmium disrupted the production of ATP, the energy currency of the cell. Drs. S. Joshi and J. Hughes have now found that cadmium binds to a mitochondrial protein (coupling factor B) discovered several years ago in Dr. Sanadi's laboratory. Further work is needed to establish the relationship between protein binding, the biological toxicity of cadmium, and ATP production. Dr. Sanadi suspects that the inactivation of mitochondrial coupling factor B may be relevant to acute cadmium toxicity encountered in industrial accidents.

Radiation and Chemicals

Environmental factors such as solar ultraviolet light, ozone, oxygen, and pollutants can change or bind to proteins, nucleic acids, and other components of tissue. Structural proteins like collagen and certain components of the lens may persist for nearly a lifetime, and any damage sustained over a lifetime may remain in those proteins. The exposed, sensitive eye is particularly likely to accumulate damage in this way. Drs. E. Fujimori and B. Srinivasan are characterizing the chemical changes induced by radiation, chemicals, and the aging process in lens protein and collagen.

THANK YOU

BBRI is extremely grateful to the individuals and institutions listed below who have made generous contributions during the past fiscal year.

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BOSTON BIOMEDICAL RESEARCH INSTITUTE
Balance Sheet
August 31, 1980 and 1979

	1980					1979
	Unrestricted Funds		Restricted	Plant	Total All	Total All
	Operating	Other	Funds	Funds	Funds	Funds
ASSETS						
Current assets:						
Cash	$ 11,865	$	$ 58,431	$	$ 70,296	$ 99,655
Grants receivable			3,328,138		3,328,138	2,887,248
Pledges receivable	25,000	1,000			26,000	105,000
Prepayments, deposits and other receivables	22,912				22,912	54,524
Investments, 1980 at market value (cost – $1,166,771), 1979 at cost (market value – $624,865)	113,129	546,613	504,835		1,164,577	641,611
Total current assets	172,906	547,613	3,891,404		4,611,923	3,788,038
Fixed assets: (See notes 1 and 2)						
Leasehold improvements				1,757,902	1,757,902	1,757,902
Research equipment				2,379,194	2,379,194	2,202,291
Furniture and fixtures				47,129	47,129	46,054
Total				4,184,225	4,184,225	4,006,247
Less accumulated depreciation and amortization				1,596,242	1,596,242	1,324,847
Net fixed assets				2,587,983	2,587,983	2,681,400
Total assets	172,906	547,613	3,891,404	2,587,983	7,199,906	6,469,438
LIABILITIES AND FUND BALANCES						
Current liabilities:						
Accounts payable	424				424	256
Accrued expenses	40,000				40,000	37,595
Overhead and fringe benefit adjustment payable			238,356		238,356	323
Total current liabilities	40,424		238,356		278,780	38,174
Fund balances: (See note 1)						
Grants and contracts			3,436,653		3,436,653	2,867,714
Operating	132,482				132,482	106,633
Equipment replacement		349,808			349,808	291,767
Permanent research		155,455			155,455	143,043
Building program		42,350	216,395		258,745	340,707
Fixed assets				2,587,983	2,587,983	2,681,400
Total fund balances	132,482	547,613	3,653,048	2,587,983	6,921,126	6,431,264
Total liabilities and fund balances	$172,906	$547,613	$3,891,404	$2,587,983	$7,199,906	$6,469,438

The accompanying notes are an integral part of these financial statements.

BOSTON BIOMEDICAL RESEARCH INSTITUTE
Statement of Revenues, Expenses and Changes in Fund Balances
For the Years Ended August 31, 1980 and 1979

	1980					1979
	Unrestricted Funds		Restricted	Plant	Total All	Total All
	Operating	Other	Funds	Funds	Funds	Funds
Revenues:						
New Grants awarded	$	$	$4,297,000	$	$4,297,000	$3,854,321
Equipment replacement			32,723		32,723	31,535
Contributions	65,558		1,278		66,836	64,454
Building Program Pledges			(100,000)		(100,000)	(100,000)
Property and equipment purchased (See notes 1 and 2)				177,978	177,978	179,870
Investment income	11,213	37,730	39,618		88,561	50,895
Miscellaneous						486
Total	76,771	37,730	4,270,619	177,978	4,563,098	4,081,561
Expenses: (by department)						
Muscle Research			1,658,049		1,658,049	1,361,419
Cell Physiology			533,931		533,931	491,108
Developmental Biology			271,086		271,086	283,565
Fine Structure			468,159		468,159	471,192
Metabolic Regulation			328,290		328,290	262,558
Bioorganic Chemistry			149,371		149,371	125,993
General Research	20,997		87,143		108,140	117,068
Fund Raising	12,497				12,497	3,492
Purchase of equipment	17,428				17,428	
Depreciation and amortization (See note 2)				271,395	271,395	251,047
Total	50,922		3,496,029	271,395	3,818,346	3,367,442
Net addition (deduction) to fund	25,849	37,730	774,590	(93,417)	744,752	714,119
Other changes in fund balances:						
Overhead adjustment			(254,890)		(254,890)	(276,023)
Added to equipment replacement fund		32,723	(32,723)			
Fund balances, beginning of year (See note 1)	106,633	477,160	3,166,071	2,681,400	6,431,264	5,993,168
Fund balances, end of year (See note 1)	$132,482	$547,613	$3,653,048	$2,587,983	$6,921,126	$6,431,264

The accompanying notes are an integral part of these financial statements.

BOSTON BIOMEDICAL RESEARCH INSTITUTE

Notes to Financial Statements
August 31, 1980

[1] - Summary of Significant Accounting Policies:

Fund Accounting

The accounts are maintained on the accrual basis and in accordance with the principles of fund accounting. Funds that have similar characteristics have been combined into the following fund groups:

* Unrestricted funds include two groups representing the portion of expendable funds available for support of operations: a) The operating fund includes unrestricted contributions and investment income less the cost of grants not reimbursed in full by granting agencies, and further reduced by transfers to other funds; b) Other unrestricted funds represent reserves transferred from the operating fund, and a building program fund derived from unrestricted contributions.
* Restricted funds represent resources restricted for research grants or building additions. Research grants are added to the fund balance when awarded, and direct charges are deducted when incurred together with the related portion of earned overhead.
* Plant funds represent the undepreciated cost of leasehold improvements, equipment and furniture and fixtures.

Other Matters

All income, gains and losses arising from the sale, collection, or valuation at market of investments are allocated to the fund owning the assets.

A portion of the overhead chargeable to research grants is deemed to be reimbursement for equipment and is shown as an addition to the Equipment Replacement Fund. This amounted to $32,723 in 1980 ($31,525 in 1979). In addition, $17,428 of computer equipment was charged to the operating fund in the year ended August 31, 1980 and added to the plant fund.

[2] - Plant Assets and Depreciation:

Boston Biomedical Research Institute, under an agreement dated June 16, 1970, shares with Retina Foundation the use of research facilities for fifty years at 20 Staniford Street, Boston, and of a research farm in Townsend, Massachusetts.

The leasehold improvement asset category represents the cost of Boston Biomedical Research Institute's long-term leasehold in the building and improvements, and is being amortized over the 50-year lease term. The furniture and equipment categories represent, at cost, acquisitions from operating funds and restricted research grant awards. Depreciation is primarily on the straight-line basis over the estimated 10 year useful life of the assets. All depreciation and amortization is charged to the plant fund.

[3] - Government Grants:

All grant costs billed to the U.S. government and most private grants are subject to audit and by the granting agency.

GREENE & COMPANY/*Certified Public Accountants, P.C.*
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Board of Trustees
Boston Biomedical Research Institute
Boston, Massachusetts

We have examined the balance sheet of Boston Biomedical Research Institute as of August 31, 1980 and the related statement of revenues, expenses and changes in fund balances. Our examination was made in accordance with generally accepted auditing standards and accordingly included such tests of the accounting records and such other auditing procedures as we considered necessary in the circumstances. We made a similar examination for the preceding year.

In our opinion, the accompanying financial statements present fairly the financial position of Boston Biomedical Research Institute at August 31, 1980, and the results of its operations and changes in fund balances for the year then ended, in conformity with generally accepted accounting principles applied on a basis consistent with that of the preceding year.

GREENE & COMPANY

October 16, 1980

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