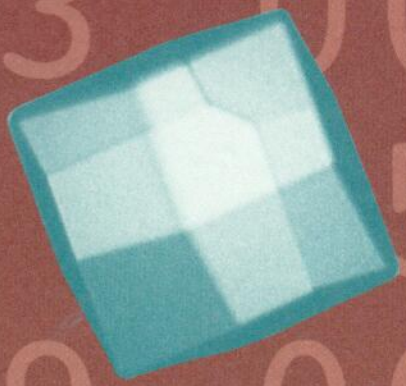
Boston Biomedical Research Institute

1997 Annual Report



About Boston Biomedical Research Institute

The Boston Biomedical Research Institute (BBRI) is dedicated to basic biomedical research to promote the understanding, treatment and prevention of specific human diseases. The areas of investigation concern the structure and function of muscle proteins, mechanisms of cell communication, and the control of cell growth and gene function. A major focus is muscle cell biology which has implications for muscle-related diseases such as hypertension, stroke, and heart failure. When appropriate, the Institute collaborates in clinical studies to apply the results of basic research to problems of human health and the cure of disease. Boston Biomedical is an independent, not-for-profit institution.

In its 27 years as an independent research organization, BBRI has established a tradition of excellence in biological research conducted in an intellectually exciting environment. BBRI's faculty consists of 25 principal investigators supported by a staff of 60 research associates, technicians, post-doctoral scientists in training, and students. While the true measure of the Institute's success is in how its work has changed people's lives, it is worth noting that BBRI ranked among the top 20 independent research institutes in the United States in terms of publications cited by other scientists. BBRI scientists have the intellectual freedom to break out of traditional academic disciplines, and investigators with diverse backgrounds and approaches can interact with each other to focus on a common research program. Scientists are encouraged to follow new paths, stimulated by these interdisciplinary interactions, in the hope of fostering unexpected discoveries.

The front cover shows a crystal of a genetically altered calcium binding protein–calmodulin, and its X-ray diffraction pattern. In the background a part of the numerical representation of the diffraction pattern is shown. *Courtesy of Dr. Zenon Grabarek's laboratory.*

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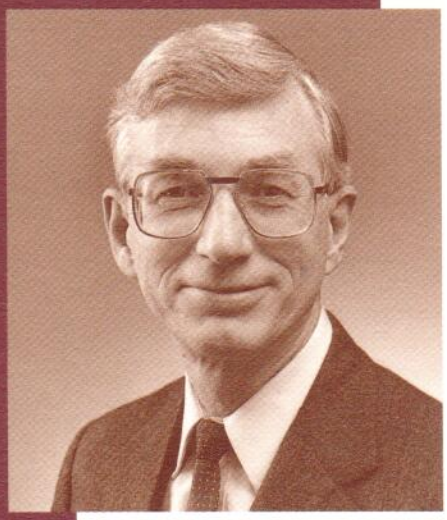
Message from the President



At our celebration party for successfully meeting the Peabody Challenge for funding an X-ray crystallography facility, Dr. Endre A. Balazs, BBRI's founding Research Director, related the following story:

In the early years of BBRI, numerous scientific advances were made by acquiring and applying the tools from other scientific fields to biological systems. During a visit to BBRI by a prominent European scientist these instruments were proudly displayed. Finally, the visitor responded, "Enough of the birdcages, tell me about the birds."

BBRI's ongoing recruitment efforts are essential not only to our continued position as leaders in the biomedical research field but also to the increasing financial security of the Institute.

While we proudly point to our achievement this year of successful implementation of the first phase of the BBRI Structural Biology Facility: the X-ray crystallography facility, the central story at BBRI is still the "birds". For this new facility Dr. Kathleen Morgan, BBRI's Director, has done a superb job in recruiting three of the most promising and recognized young crystallographers in the country. We anticipate having the crystallography facility running and available to all BBRI scientists by the fall of 1997.

In our Five-Year Strategic Plan, we implemented a recruitment program that would bring two new scientists each year to the institute, with the expectation that each new recruit would secure independent funding (federal or otherwise) within two years. To date, BBRI's recruitment efforts have been highly successful: of the four new scientists recruited in the past two years, three have received funding of almost $3.3 million (over a five year period), and the fourth has an application under review at NIH that has an excellent chance of being fully funded.

BBRI's ongoing recruitment efforts are essential not only to our continued position as leaders in the biomedical research field but also to the increasing financial security of the Institute. The continued willingness of high potential young scientists of enormous creative energy and confidence in their ability to succeed to accept the risk of joining an independent research institute is truly inspiring. Through the generous gifts of BBRI's supporters which cover the costs of supporting young scientists, equipping a laboratory, and providing interim funding when a grant is delayed – costs not covered by grants – BBRI will maintain the flexibility and intellectual environment only provided by an independent research institute.

David A. Gibbs

Message from the Director

As any of the volunteers, scientists and staff that have worked at the BBRI this last year will tell you, it has been a good year.

We have been exceptionally fortunate to have received a challenge grant from the Amelia Peabody Charitable Fund that made feasible the establishment of an X-ray crystallography facility, which is a cornerstone of our five-year Strategic Plan. We have been equally fortunate in having a devoted group of sophisticated supporters who had the insight to recognize the value of this "high-tech" opportunity and helped us meet the challenge.

Having available the required $0.5 million required to purchase state-of-the-art X-ray crystallography equipment allowed us to attract an exceptionally strong group of applicants for this year's faculty recruitment efforts and to succeed in recruiting our top choices from those applicants.

As a cell biologist, I look forward with great anticipation to the new insights to be gained in protein-protein interaction and cell function from the structures that our new scientists are hoping to solve.

These three scientists, Drs. Andrew Bohm, Roberto Dominguez and Celia Harrison come from leading crystallography labs at Yale, Brandeis and Rockefeller University and will be setting up laboratories at the BBRI that nicely fit our three areas of scientific focus – signal transduction, motility and cell growth. You will read more about these bright young scientists in the pages that follow.

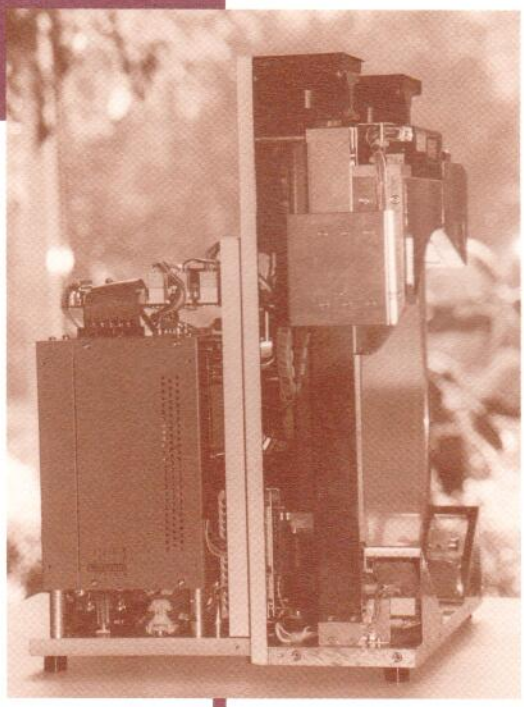
The addition of the on-site X-ray crystallography facility and these three new crystallographers to the on-going crystallography program of Dr. Zenon Grabarek gives the BBRI a remarkable concentration of strength in this field and builds beautifully on our historical reputation of excellence in the area of protein structure. As a cell biologist, I look forward with great anticipation to the new insights to be gained in protein-protein interaction and cell function from the structures that our new scientists are hoping to solve. Our non-scientist supporters have also been impressed by the potential of this molecular information in rapidly pointing the way for the design of therapeutic molecules as well as being delighted by the fundamental aesthetic appeal of these atomic structures. I hope you are equally delighted – and thank you for your support!

Kathleen G Morgan

Kathleen G. Morgan

X-ray Crystallography at BBRI – Challenges and Opportunities

One of the thrills of doing biomedical research is that our curiosity is never fully satisfied but is constantly piqued by new problems. When we find an answer to an important question, we are gratified but cannot sit back complacently, for we immediately perceive new questions that lie embedded in our answer and demand a solution. The contributions of BBRI scientists to the understanding of muscle contraction illustrates this process: In the early 1970's, it seemed that muscle contraction could be understood in terms of the chemical composition of muscle proteins. When this was elucidated, it became clear that it was the spatial relationship between muscle proteins that needed to be defined. When sophisticated tools were developed to measure the distances between specific atoms both within and between protein molecules, it became clear that it was necessary to know the positions of all atoms of muscle proteins. This is why BBRI scientists are now turning to X-ray crystallography, a technique that has undergone rapid maturation and makes it possible to analyze the 3-dimensional structure of proteins with resolution at the atomic level.



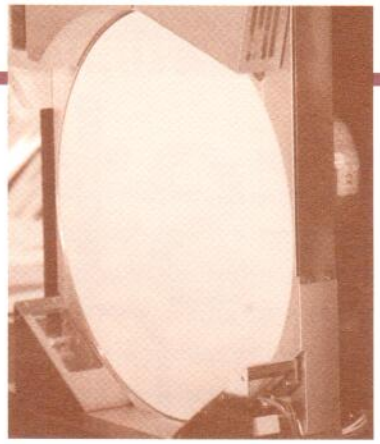
What is X-ray Crystallography?

A **crystal** is a 3-dimensional array of molecules, arranged in a repeating pattern. For example, a salt crystal consists of sodium chloride (NaCl) molecules arranged in a such way that sodium and chloride atoms occupy alternating corners of a cube. The salt crystal is thus essentially a stack of molecular cubes. Indeed, if we look carefully at a crystal of table salt, we can recognize the cubic shape that reflects its molecular structure. In the same way as salt crystals form when the water in which the NaCl is dissolved evaporates slowly, crystals of much more complex molecules such as proteins can be induced to form by a slow process of dehydration. However, making perfect protein crystals is not only an experimental skill but an art, and good crystallographers are often judged by their "luck" in growing protein crystals.

Because the molecules that constitute a crystal are arranged in an orderly pattern, they will "diffract" X-rays passing through the crystal so as to yield **diffraction patterns**. We can see an example of a diffraction pattern on

a rainy evening when we look at a street light through our wet umbrella. Instead of an image of the street light, we see a crossed pattern of tiny spots, which is a diffraction pattern created by the light passing through the regular weave of the umbrella fabric. A diffraction pattern is formed only when the wavelength of the light or other radiation that passes through a crystal is about the same as the spacings between the regularly arranged objects. Whereas visible light can be diffracted by the fibers of umbrella fabric, we need radiation of much shorter wavelength to obtain diffraction from atoms in a protein crystal. X-rays are ideally suited for this purpose, because their wavelength is similar to the interatomic distances in proteins.

If we measure the relative positions of the many spots of light in a diffraction pattern, we can calculate the spacings between the objects that caused the light to diffract and deduce their structure, be it the arrangement of silk fibers in our umbrella or the arrangement of atoms in a sodium chloride crystal or in a protein. However, solving the structure from the diffraction pattern



involves exceedingly complex mathematical operations, especially when we deal with protein crystals, where each molecule consists of many thousands of atoms, and requires high-powered computers and sophisticated software. Indeed, the major advances in X-ray crystallography in the past 10 years have been in the computational methods used for deducing complex protein structures at atomic resolution.

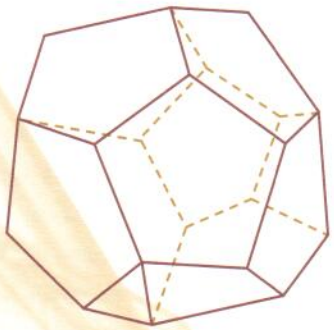
New Research Opportunities

The application of X-ray crystallography to specific research problems at BBRI was pioneered by Principal Scientist Zenon Grabarek. Zenon crystallized genetically altered forms of the regulatory protein calmodulin and began their crystallographic analysis, using the X-ray crystallographic facility at Boston University. However, it soon became evident that the intensive crystallographic investigations envisioned in BBRI's strategic plan would require an in-house X-ray crystallographic facility. Accordingly, an all-out effort was made to raise $0.5 million for the purchase of the instrumentation and computer facilities to meet this urgent need. As mentioned elsewhere in this Annual Report (see the Director's message and Development report), BBRI was fortunate to receive a challenge grant from the Amelia Peabody Charitable Fund and the necessary matching funds through the outstanding efforts and generosity of the members of BBRI's Board of Trustees and Corporation, enabling BBRI to purchase the necessary X-ray crystallography equipment.

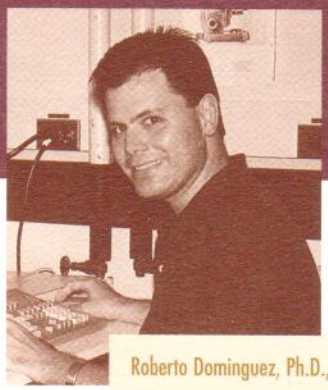
The availability of a state-of-the-art X-ray crystallography facility placed BBRI in a strong position to recruit scientists who already had made their mark as X-ray crystallographers. When BBRI announced a competition for a faculty position in X-ray crystallography, the Search Committee was overwhelmed by the large number of excellent applicants, many of whom had already made significant contributions to one of BBRI's major focus areas: motility, signal transduction, or cell growth. It was most gratifying that our top candidates in each of these areas, who were offered faculty positions, accepted the offers and have already joined the BBRI research effort or will do so within the next 6 months. Some of the research accomplishments and plans of these three new faculty members, Drs. Roberto Dominguez, Andrew Bohm, and Celia Harrison, are briefly described in the pages that follow.

crystal

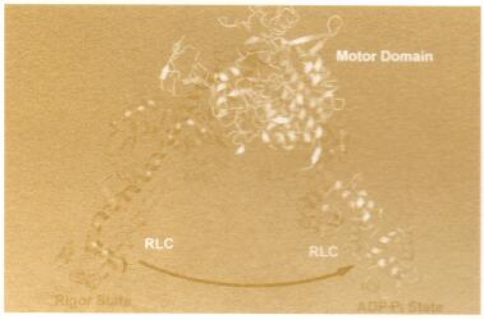
A crystal is a 3-dimensional array of molecules arranged in a repeating pattern. Even large molecules containing thousands of atoms can be crystallized.



Motility – Roberto Dominguez



Roberto Dominguez, an experienced crystallographer with a very strong background in the mathematical aspects of solving crystal structures, is just completing a postdoctoral research fellowship in the Rosenstiel Basic Medical Sciences Research Center at Brandeis University. One of his research problems is the X-ray structure determination of troponin C fully complexed with calcium. Troponin C is an important regulatory protein in skeletal and heart muscle that was first characterized at BBRI, and its structure and function is profoundly affected by the binding of calcium to two regulatory sites. It is the molecular switch that senses increases in calcium levels and – in heart cells – initiates the heart beat.



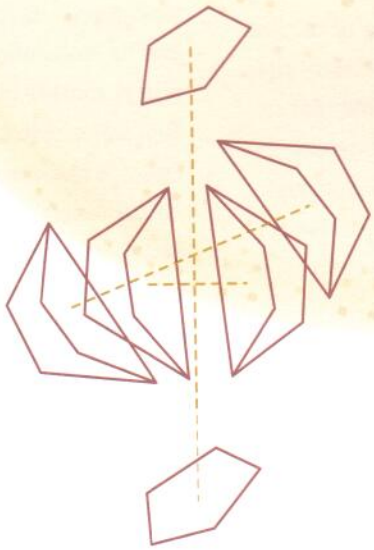
Another research problem is the structure of the "motor domain" of smooth muscle myosin. Smooth muscle contains two main proteins, actin and myosin. The actin molecules are laid out like tracks in long filaments along which the myosin molecules, which are miniature chemical motors, can move. The movement of myosin along actin leads to the contraction and narrowing of blood vessels which causes blood pressure to rise. Roberto's 3-dimensional structure of the myosin motor domain, together with the essential myosin light chain, which is shown on this page, allows us to visualize the molecular movements. It provides clues to the unusual properties of smooth muscle myosin and should help us understand such serious pathological conditions as hypertension and coronary artery spasm.

When he establishes his laboratory at BBRI next March, Roberto plans to focus primarily on regulatory aspects of muscle contraction, with particular emphasis on smooth muscle proteins. One project will be a collaboration with Zenon Grabarek to study the structural basis of the interaction of calmodulin with several different target proteins and its modulation by calcium. Calmodulin is another important calcium-dependent switch. A major calmodulin target is the enzyme myosin light chain kinase, which in turn, controls smooth muscle contraction. Yet another project is the elucidation of the 3-dimensional structure of myosin I in collaboration with Principal Scientist Lynne Coluccio. Myosin I is a special form of myosin which is also found in non-muscle cells and appears to function in cell motility and intracellular transport processes.

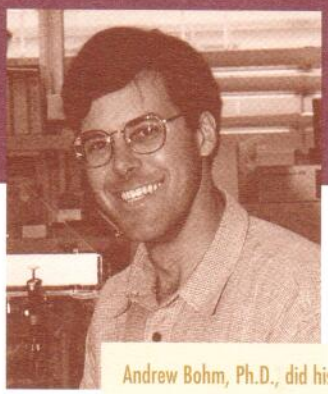
Roberto Dominguez, Ph.D., began his scientific career pursuing, first a Masters of Physics in theoretical physics & mathematics at Odessa University in the former USSR, and later a Ph.D. – with highest distinction – in macromolecular X-ray crystallography at the Pasteur Institute in Paris. In his native Cuba, Roberto worked at the Center for Genetic Engineering and Biotechnology (CIGB) where he was involved in software development for protein sequence alignment and protein engineering. Roberto was awarded fellowships in both Germany and Belgium, studying in both countries. During his postdoctoral studies at the Rosenstiel Center at Brandeis University, with Dr. Carolyn Cohen and in collaboration with Dr. Kathy Trybus, he became fascinated with the area of "molecular motors", specifically in the smooth muscle cells of blood vessels. The solution of the 3-dimensional structure of this myosin motor, determined via X-ray crystallography, will provide a clue to many of the unusual properties of smooth muscle myosin, thus helping scientists to understand such conditions as hypertension and coronary artery spasm. This interest, combined with his past biotechnology experience, has left him with a long-term interest in bringing his fundamental molecular insights to the stage of pharmaceutical and medical applications.

X-ray diffraction

When X-rays pass through a crystal a diffraction pattern is formed that is characteristic of the 3-dimensional arrangement of all the atoms in the crystal.

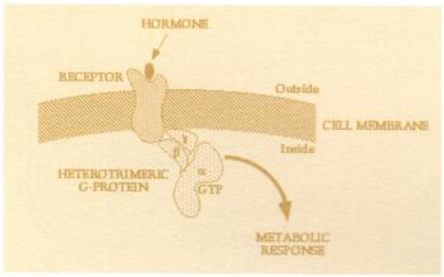


Signal Transduction – Andrew Bohm



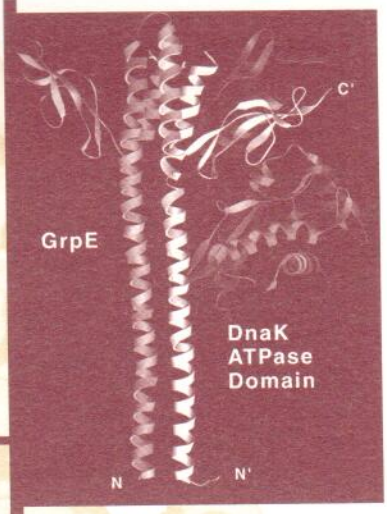
Andrew Bohm, Ph.D., did his undergraduate work at the State University of New York at Binghamton, where he majored in biochemistry and did research in neurobiology. After a year as a research assistant at the Public Health Research Institute of New York, working with animal cells and viruses, Andrew decided to pursue graduate studies in biophysics at the University of California in Berkeley. His research was done in the laboratory of Dr. Sung-Hou Kim. His Ph.D. thesis involved crystallizing and solving the structure of the human macrophage colony stimulating factor, an important regulator of the immune response. Andrew continued at Berkeley for two postdoctoral years, during which time he continued his work on macrophage colony stimulating factor and also contributed to the crystallographic structure solution of a hammerhead catalytic RNA and the yeast heat shock transcription factor. Andrew then moved on to the Howard Hughes Medical Institute at Yale University, where he joined Dr. Paul Sigler's research group to solve the 3-dimensional structure of proteins involved in signal transduction. Most remarkable about Andrew's research career are the broadness of his interests and his effectiveness in collaborating with other research groups, attributes which will be much valued in BBRI's interactive research environment.

Andrew Bohm's current research as a postdoctoral fellow at the Howard Hughes Medical Institute at Yale University focuses on the structure of proteins known to scientists as "heterotrimeric G-proteins", which play a key role in signal transduction. Signals such as hormones activate cells by binding to cell surface receptors, which extend through the cell membrane into the interior of the cell. At the inner side of the cell membrane, the receptors interact with G-proteins, which are composed of three different subunits (hence, the term "heterotrimeric"), causing them to bind a substance known as GTP (hence, the term "G-protein"). This, in turn, triggers a structural change in the G-proteins and sets in motion a complex cascade of reactions that ultimately translate into a final cellular response, as shown in the diagram above. Andrew is investigating G-proteins in the rod-cells of the eye which are involved in the transduction of a light stimulus into a nerve impulse. This neural response to light is attenuated under very bright conditions, a phenomenon termed "light adaptation", by the interaction of a protein known as "phosducin" with the β and γ subunits the G-protein. Andrew and his colleagues at Yale have recently solved the structure of the G-protein β and γ subunits complexed with phosducin. The G-protein has a very striking propeller-like structure with seven blades, which is illustrated in the figure on the previous page. Ordinarily, G-proteins are associated with the cell membrane where they receive signals from rhodopsin, the light-sensing molecule. However, Andrew's structure of the G-protein – phosducin complex shows that phosducin interacts with the membrane binding portion of the G-protein (at the bottom of the figure), thereby interfering with its function and attenuating the response to light.



When he establishes his laboratory at BBRI this fall, Andrew will focus on the modulation of signal transduction by G-proteins associated with ß-adrenergic receptors. These receptors respond to stress hormones such as adrenaline and therefore play an important role in human physiology and behavior. In heart cells, the interaction of adrenaline with this molecular complex is an important determinant of the rate and force of the heart beat. An understanding of the molecular mechanisms by which the stress response can be attenuated may guide the development of important new classes of heart drugs.

structure

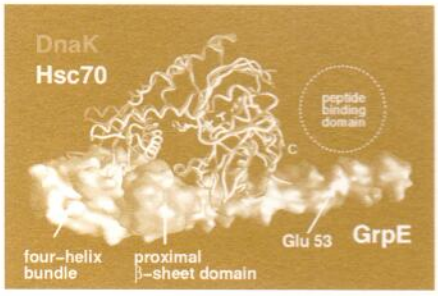


Solving the structure of a protein from the X-ray diffraction pattern involves complex mathematical operations.

Cell Growth – Celia Harrison

The research career of Dr. Celia Harrison is distinguished by excellence and a pioneering spirit. After earning her B.S. degree magna cum laude, from Pacific Lutheran University in Tacoma, Washington, Celia went on to graduate studies at the University of California in Berkeley. She chose a new faculty member, Dr. Hillary Nelson, as her Ph.D. thesis advisor, to pursue crystallographic studies of a heat shock transcription factor from yeast. This meant trying to get crystallographic research done from scratch without any X-ray equipment for the first few years, but Celia obtained crystals and solved their structure in a remarkably short time. For her postdoctoral work, Celia moved to the Howard Hughes Medical Research Institute at Rockefeller University, where she and her sponsor, Dr. John Kuriyan, entered into a fruitful collaboration with Dr. Ulrich Hartl of Memorial Sloan-Kettering Cancer Center to study the 3-dimensional structures of bacterial heat shock proteins. These proteins play an important role in the folding of intracellular proteins, as well as their refolding after damage by heat or other environmental stresses. This structure, too, was solved in very short order, thanks to Celia's artistry in obtaining crystals and her talents as an X-ray crystallographer. Indeed, Celia's originality, independence, and expertise in all aspects of protein structure determination will be a great asset to BBRI when she joins the Institute's faculty in late fall.

Celia Harrison comes to BBRI from a postdoctoral fellowship at the Howard Hughes Medical Institute at Rockefeller University. Her research focuses on the structure and function of molecular chaperones, also known as heat shock proteins, which play an important role in the folding of intracellular proteins as well as their refolding after damage by heat or other environmental stresses. The normal growth of cells and their survival under stress depends on the presence of these chaperone proteins. The mechanism by which molecular chaperones refold proteins is rather complex and to some extent controversial. An especially interesting aspect is how protein refolding is driven by the binding and hydrolysis of ATP by the chaperones. Celia and her colleagues at Rockefeller University have been studying a chaperone protein called DnaK, which functions in cooperation with another protein, GrpE. They have solved the structure of the DnaK-GrpE complex, which is shown in the figure on the previous page. These structural studies pave the way for studies on the mechanism by which the interaction of DnaK with an unfolded protein is modulated by ATP hydrolysis and the binding of GrpE so as to promote proper protein folding by successive dissociation-reassociation cycles. Understanding the 3-dimensional structure of the molecular chaperones should help us understand the way in which other proteins are folded into their 3-dimensional configuration.



Celia's structural studies on molecular chaperones will be a valuable complement to the studies by Staff Scientist Michael Sherman at BBRI on similar proteins in animal tissue and their role in the recovery from oxidative stress brought about by heart attacks and stroke. The elucidation of the structure of molecular chaperones and the complexes in which they function and which modulate their activity will give important insights on how to reduce ischemic damage to the heart and other tissues.

Development Report

This fiscal year at BBRI has been one of the most challenging for fundraising – as well as one of the most exciting and successful! As the new chair of the Development Committee, I am pleased to announce that we were successful in meeting the Peabody Challenge special fundraising campaign, and also have continued this wonderful momentum and raised – in addition –$291,000 for BBRI's Annual Fund. I know I speak for all members of the Development Committee when I say a very sincere and appreciative "thanks" to everyone who provided such enthusiastic and valuable financial support of these two fundraising programs.

The Peabody Challenge

Last year BBRI received a challenge grant from the Amelia Peabody Charitable Fund to raise funds for the first phase of BBRI's Structural Biology Facility: an X-ray crystallography facility. Of the $500,000 needed to purchase the equipment, the Peabody Fund indicated they would give BBRI $200,000 if we raised the additional $300,000 by December 1, 1996 – which we did! The implementation of the Structural Biology Facility is now underway, with the purchase of the equipment and recent recruitment of three new scientists to run the facility. This is a significant achievement for BBRI, not only in the fundraising efforts, but also as a major enhancement of BBRI's scientific programs. Many, many thanks to everyone who supported this special campaign!

BBRI Annual Fund

BBRI's fiscal year 1997 Annual Fund presented an interesting challenge to the members of the Development Committee, as we worked diligently to ensure that donors to the Institute supported both The Peabody Challenge as well as the Annual Fund for this year – and again, we were successful!

As BBRI grows, and strengthens its position as a leader in the field of basic biomedical research, our roles as fundraisers and donors become even more critical to the continued success of the Institute. Perhaps the most important goal for the 1998 fiscal year is to broaden our donor base – a challenge that will require everyone's effort. My very sincerest appreciation to everyone who supported our exciting campaigns this year – following is a list of our donors – and, with your continued commitment, I know we will achieve our goals in the future.

Allie Blodgett
Development Committee Chair

Fiscal Year 1997 Donors

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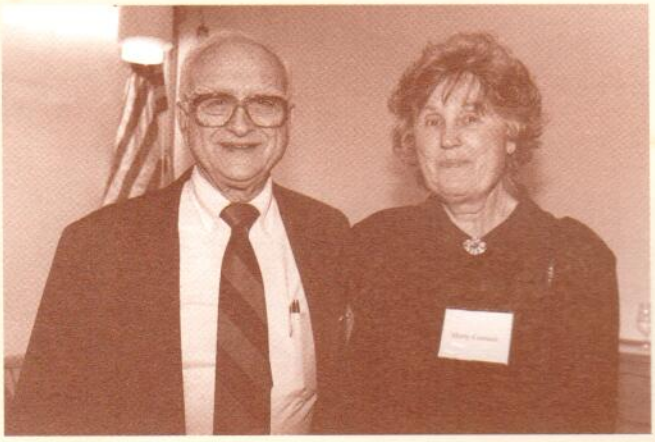

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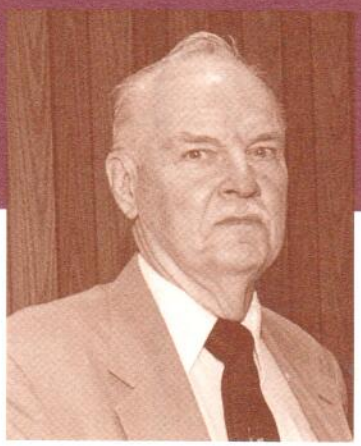
Treasurer's Report



Of particular note in BBRI's financial statements is the change in fiscal year end from August 31 to June 30. There was unanimous consensus on the Board of Trustees that BBRI's year end should coincide with most major not-for-profit scientific organizations, and that it would benefit the Institute's fundraising efforts to have June 30 as the date of fiscal close.

As we begin the second full year of implementation of the Five-Year Strategic Plan and Financial Forecast, we have the opportunity to reflect on financial matters past, present and future. BBRI continues to have three primary sources of revenue: faculty-initiated grants, return on investments, and voluntary contributions.

Board members, corporators, foundations and individuals met the challenge of a local Boston foundation and raised over $500,000 to develop an X-Ray crystallography facility at BBRI, the cornerstone Phase One achievement of BBRI's Structural Biology Facility.

Grants from the National Institutes of Health (NIH) continue to be the major source of funding, with NIH grants representing approximately 85% of total grant revenue. We still have a long-term goal of increasing revenue by building upon our solid foundation at NIH and seeking alternative sources of grant revenue from organizations such as the National Science Foundation and American Cancer Society. Meanwhile the Patents and Technology Committee continues its efforts to find collaborative opportunities with biotechnology companies; these collaborations should help deliver discoveries found through basic science to the commercial marketplace and health care facilities.

Fiscal 1997 was a tremendous year for capital expansion of scientific equipment. Faculty members generated equipment grants and corporate donations in excess of $500,000 resulting in the purchase of an ultracentrifuge and a mass spectrometer. Board members, corporators, foundations and individuals met the challenge of a local Boston foundation and raised over $500,000 to develop an X-Ray crystallography facility at BBRI, the cornerstone Phase One achievement of BBRI's Structural Biology Facility.

BBRI's investment portfolio had an overall return of 24% which generated over $2,000,000 in new funds. This gain was made possible by key investment strategies initiated within the Investment Committee in consort with the overall growth in the economy. This gain more than offset the operating loss for the shortened fiscal year.

In addition to generating over half a million dollars for the X-Ray crystallography facility, donors continued to support the BBRI Annual Fund with gifts totaling $291,000. The Development Committee's efforts, especially those put forth by the Chair, Allie Blodgett, are to be commended.

The Board of Trustees and management continue to monitor the progress of the strategic plan while fine tuning it as knowledge and experience grows. I look forward to another year in my capacity as Treasurer and challenge all of my fellow Board members to continue to provide advice and support to BBRI's tremendous growth and progress.

Respectfully submitted,
Ernest Henderson, III
Treasurer

Statements of Financial Position

June 30, 1997 and August 31, 1996

Assets	1997	1996
Cash	$ 718,342	$ 188,115
Grants receivable	2,916,957	3,122,380
Pledges receivable	90,191	–
Investments	8,238,723	7,512,420
Prepayments, deposits and other receivables	136,707	25,421
Property and equipment	1,617,075	1,145,396
Deferred compensation investments	1,554,891	1,220,186
Total assets	$ 15,272,886	$ 13,213,918
Liabilities and Net Assets		
Accounts payable and accrued expenses	$ 156,613	$ 99,969
Deferred income	3,018,464	3,679,983
Deferred compensation payable	1,554,891	1,220,186
Total liabilities	4,729,968	5,000,138
Net Assets		
Unrestricted	9,287,600	7,599,664
Temporarily restricted	859,175	292,704
Permanently restricted	396,143	321,412
Total net assets	10,542,918	8,213,780
Total liabilities and net assets	$ 15,272,886	$ 13,213,918

Copies of our complete, audited financial statements, certified by the independent accounting firm Quin, Rickard, Vecchi & McCafferty, P.C., Certified Public Accountants, are available upon request from the Chief Financial Officer, Boston Biomedical Research Institute.

Statements of Activities

For the ten months ended June 30, 1997 and the year ended August 31, 1996

Changes in Unrestricted Net Assets	1997	1996
Revenues:		
Grants and contracts	$ 4,400,559	$ 5,096,527
Contributions	280,888	303,691
Investment income	1,859,970	556,968
Other income including licensing fees	241,667	16,777
Total unrestricted revenues	6,783,084	5,973,963
Net assets released from restrictions	67,453	118,724
Total unrestricted support	6,850,537	6,092,687
Expenses:		
Salaries and benefits	3,487,294	4,308,640
General support and services	878,256	1,156,616
Occupancy costs	572,483	998,536
Depreciation	169,458	206,512
Fund raising	55,110	66,109
Total expenses	5,162,601	6,736,413
Increase (decrease) in unrestricted net assets	1,687,936	(643,726)
Changes in Temporarily Restricted Net Assets		
Contributions	514,724	17,336
Investment income	119,200	28,889
Net assets released from restrictions	(67,453)	(118,724)
Increase (decrease) in temporarily restricted net assets	566,471	(72,499)
Changes in Permanently Restricted Net Assets		
Investment income	74,731	21,412
Increase in permanently restricted net assets	74,731	21,412
Increase (decrease) in net assets	2,329,138	(694,813)
Net assets at beginning of year	8,213,780	8,908,593
Net assets at end of year	$ 10,542,918	$ 8,213,780

Grants and Fellowships

Research Grants

National Institutes of Health			
Dr. Adam	MAPK in the contractile phenotype of smooth muscle	3/96 - 2/01	$1,111,000
Dr. Badwey	Enzymes modulating second messengers in neutrophils	4/93 - 3/98	639,000
Dr. Badwey	A novel signaling pathway in neutrophils	5/96 - 4/00	777,000
Dr. Gergely (MERIT)	Biochemistry of muscle contraction	7/89 - 10/97	2,733,000
Dr. Graceffa	Smooth muscle and non-muscle caldesmon	5/93 - 4/98	748,000
Dr. Ikemoto	Structure and function of sarcoplasmic reticulum	9/96 - 8/01	2,380,000*
Dr. Lehrer	Tropomyosin and myosin interaction in muscle	12/95 -11/00	2,044,000
Dr. Lehrer	Cooperative effects in smooth muscle regulation	5/97 - 3/02	885,000*
Dr. Lu	Voyager TM Elite biospectrometry research station	4/97 - 4/98	162,000*
Dr. Morgan	Regulation of contraction and growth of blood vessels	7/96 - 6/99	713,000
Dr. Morgan	Contraction of vascular smooth muscle cells	4/95 - 3/97	327,000
Dr. Morgan	Contraction of vascular smooth muscle cells	4/97 - 3/01	768,000*
Dr. Paulus	Control of diaminopimelate and lysine biosynthesis	4/93 - 3/98	1,202,000
Dr. Paulus	Mechanism of protein splicing in mycobacterium	4/97 - 3/01	1,377,000*
Dr. Sarkar	Function of polyadenylate sequences in bacterial RNA	12/93 -11/97	1,211,000
Dr. Sherman	Molecular chaperones and protein phosphorylation	5/96 - 4/00	1,068,000
Dr. Tao (MERIT)	Proximity relationship among muscle proteins	5/96 - 3/00	2,165,000
Dr. Volloch	Globin mRNA hyperproduction in response to anemia	11/96 -11/97	89,000*
Dr. Wang (Pro. Proj.)	Molecular mechanism of smooth muscle regulation	9/92 - 8/97	6,790,000
Dr. Wang	Caldesmon and transmembrane signaling	9/93 - 9/96	60,000
Dr. Wohlrab	Proton-coupled inorganic phosphate transport	4/92 - 3/98	1,231,000
Alzheimer's Association			
Dr. Volloch	Molecular mechanism of ß-amyloid overproduction in Alzheimer's disease	4/97 - 3/00	150,000*
Defense Advanced Research Projects Agency			
Dr. Leavis	Embryonal factors as antiinfective agents	2/97 - 1/00	844,000*
American Cancer Society			
Dr. Coluccio	Myosin-I in liver	4/96 - 12/97	187,000
Dr. Sherman	Role of Hsp70 in ubiquitin-dependent proteolysis	12/95 - 11/96	35,000
Medical Foundation			
Dr. Sherman	Molecular chaperones and degradation of oxidatively damaged protein	7/96 - 6/98	100,000
Muscular Dystrophy Association			
Dr. Ikemoto	Excitation-contraction coupling in malignant hyperthermia	7/94 -12/97	130,000
National Science Foundation			
Dr. Stafford	XL-A Analytical ultracentrifuge for the analysis of protein- protein interactions	3/96 - 2/98	158,000
Dr. Lu	MALDI-TOF Mass spectrometer	4/97 - 3/99	113,000*
Sponsored Research			
Dr. Stafford	Analytical ultracentrifugation	5/97 - 4/98	60,000*

Fellowships

Dr. D'Angelo	National Institutes of Health	3/96 - 2/99	71,500*
K. Shingledecker	New England Biolabs	9/96 - 8/97	15,000*

*New grants in fiscal 1997

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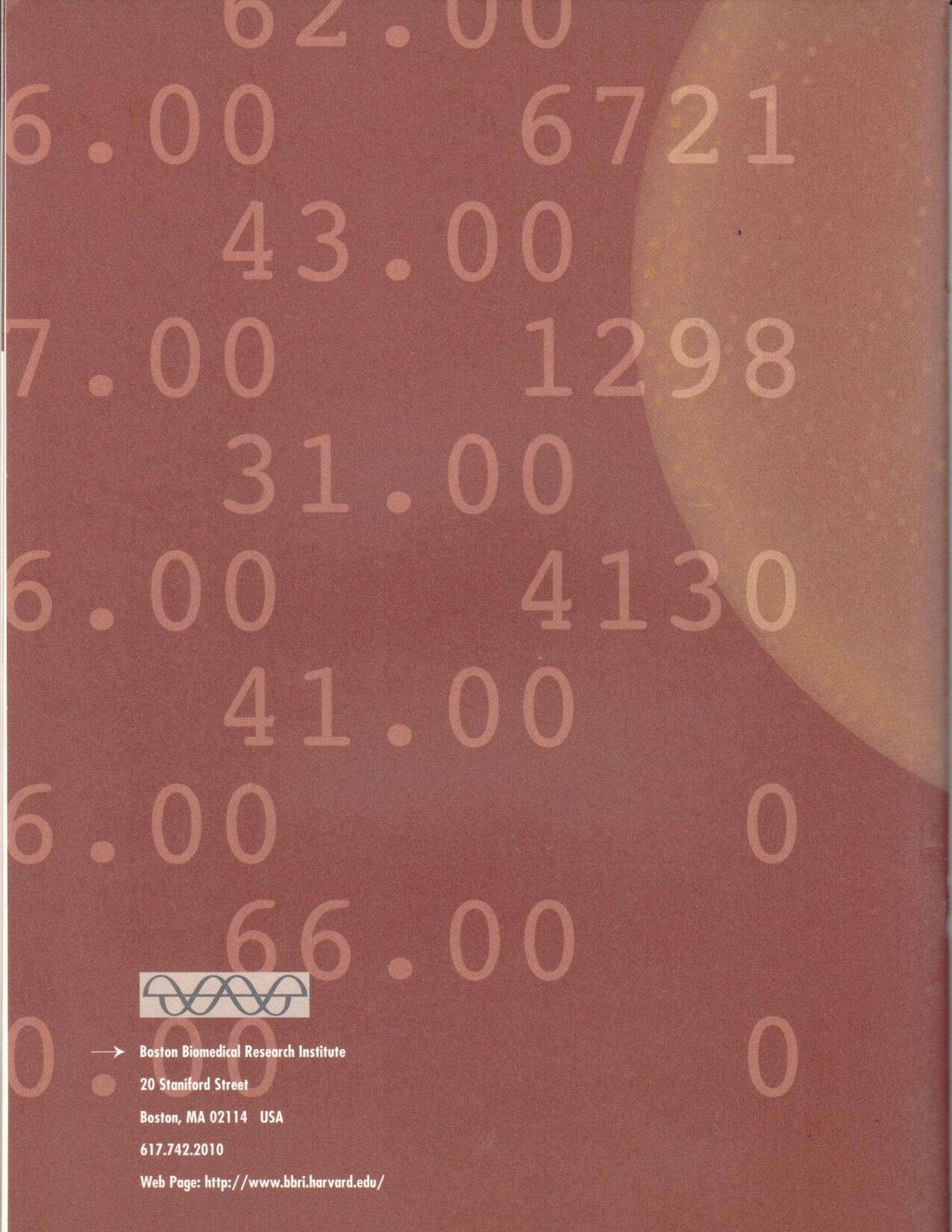

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