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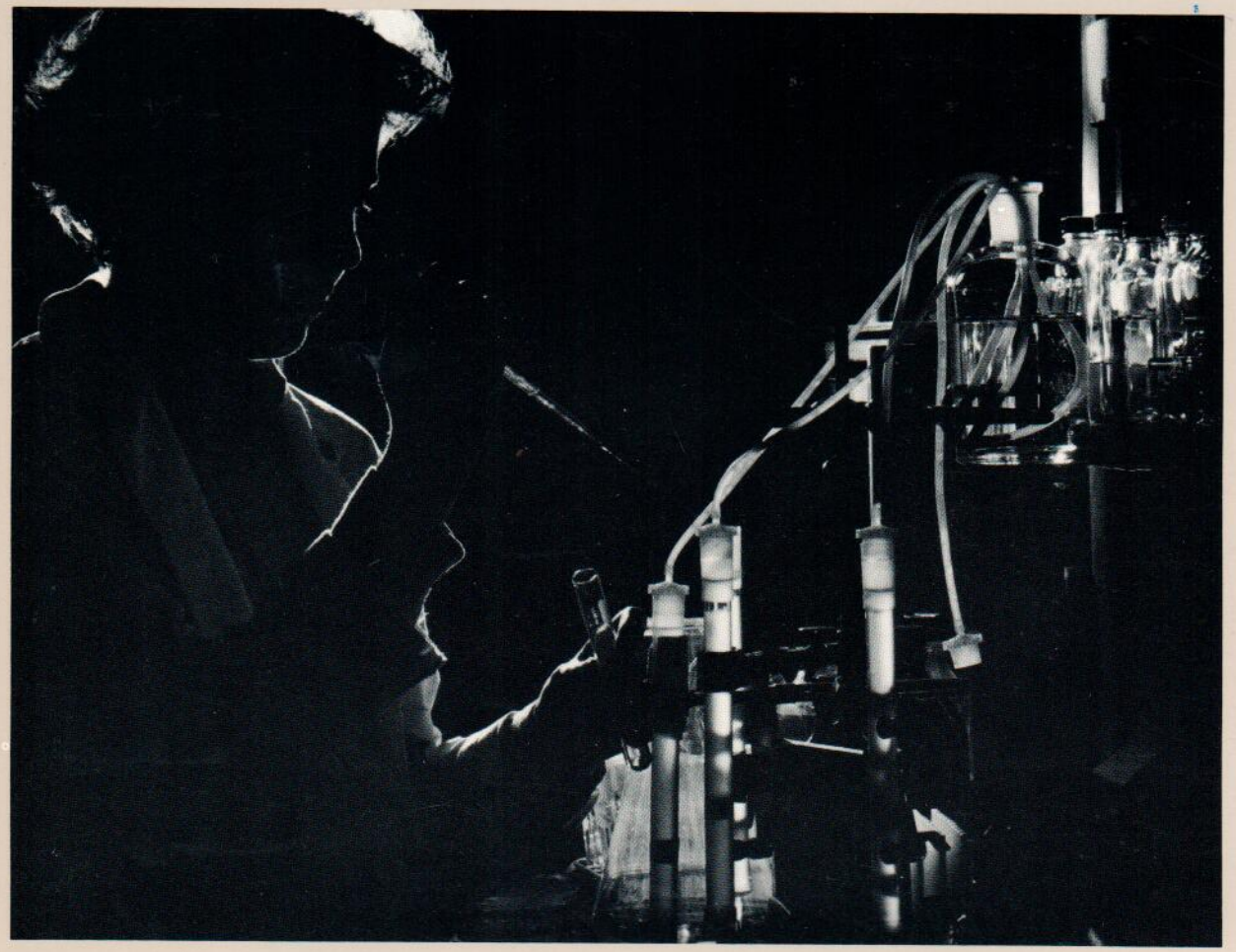
RESEARCH
INSTITUTE



1986 ANNUAL REPORT

"I believe that the major research effort, and far and away the greatest investment for the future, must be in the broad area of basic biological science. Here and there, to be sure, there will be opportunities for productive applied science, comparable, say, to the making of polio vaccine or the devising of multidrug therapy for childhood leukemia, but these opportunities will not come often, nor can they be forced into existence before their time. The great need now, for the medicine of the future, is for more information at the most fundamental levels of the living process."

— Lewis Thomas, M.D.

Boston **B**iomedical **R**esearch **I**nstitute is an independent, non-profit organization with a staff of M.D. and Ph.D. investigators who carry out a broad program of basic research in biology and medicine, and provide highly specialized training for future physicians and scientists. For over a decade the Institute has maintained its position among the leaders in the world-wide effort to prevent and cure disease. Areas currently under investigation range from the study of birth defects to the biology of aging. The findings of Institute scientists are used by others in clinical projects including those aimed at helping people suffering from cancer and diseases of the heart, muscles, liver, and eye. The Institute's research programs will ultimately bring lasting benefits to the future well-being of mankind.

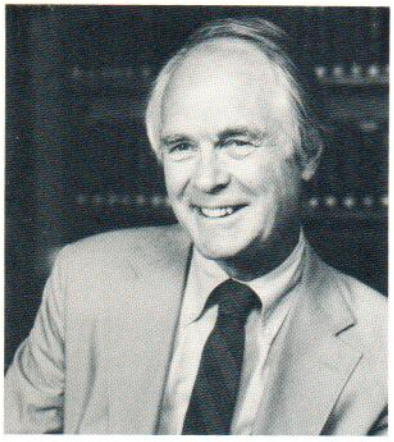
Report of the President

In conjunction with the emphasis of this year's report on the work of John Gergely and his colleagues in the field of muscle research, it is most appropriate to report that John has quite recently received an important recognition of his work. Early this summer, John received one of the first National Institute of Health MERIT awards, which assures long-term stable research support for ten years. The announcement of the award took note that John's "reputation as a leader in the field of muscle biochemistry has been recognized nationally and internationally for several decades." We are delighted both for John and the Institute that he has been honored in this fashion.

Long-term funding commitments of this sort are a form of job security we cannot regularly offer to our staff. This is a troublesome situation which needs improving; it is one of the most important long-range matters with which the Trustees have to deal. Our annual appeal, while essential to cover important non-funded and non-reimbursable costs, can offer very limited help in providing for staff salaries. While the staff continues its outstanding record in obtaining funding for the Institute's basic research projects—which includes staff salaries—this is a less than ideal way to provide for stability in compensating valued faculty. One long-term approach would be to seek ways to increase our endowment to provide annual funds to apply to faculty salaries.

While raising our sights to future funding needs, we must not overlook the present. Our Development Committee has spearheaded another record year of annual giving, $175,775—an increase of $22,646 over last year. While all donors have been separately thanked, we can now thank them again for participating in a record year!

In closing, I would like to thank the Members of the Corporation and the Board of Trustees whose term of service ended during the past year. Gilbert L. Steward, Jr. and John Trefry retired as Trustees, and Herbert Bremner, Wesley M. Dixon, Jr., Jerome Gross, James J. Meyers, Mrs. George Poor, Lloyd D. Taylor, and Barbara E. Wright retired as Members of the Corporation. Their efforts on behalf of the Institute and their contributions to its continued success have been many and are much appreciated. We hope and expect they will remain strong friends of BBRI.



John B. French

Report of The Executive Director

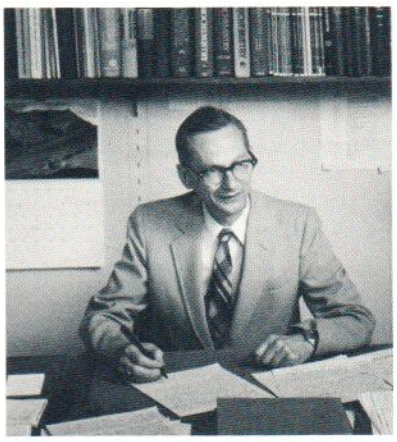
This year's report concentrates on a single area, muscle research, in which this Institute has achieved international renown. Under the leadership of John Gergely, an interdisciplinary group of scientists has studied muscle from diverse points of view, making fundamental contributions to our knowledge of how this important tissue functions. I hope that this report will not only give you an overview of a fascinating biological problem but also an insight of how BBRI's flexible organization encourages the collaboration of scientists from different disciplines with unusually productive results.

The unique atmosphere which has evolved at BBRI to give research precedence over all other interests has served basic research well, not only in the study of muscle but in many other fields. For example, BBRI has kept well abreast the revolution in molecular genetics, and the contributions by its scientists to that field are known world-wide. In this connection, I am pleased to report that BBRI has just entered into a 3-year agreement for research collaboration with the Laboratory of Molecular Genetics of the Chinese Academy of Sciences in Shanghai. We are looking forward to sharing with our Chinese colleagues our expertise in modern biology.

An objective measure of scientific success is the number of research reports published by BBRI scientists in top-ranking scientific journals, which exceeded 50 in the past year. At the same time, research grants received by BBRI increased by 15%, a remarkable growth in a fiscal year in which federal support for basic biomedical research was constrained by the necessity to reduce the budget deficit. The Institute is indeed fortunate to have been able to attract and maintain a scientific faculty of the caliber to compete so successfully for research funds.

However, this is not a time for complacency. In the years to come, the need to contain the growth of the federal budget will undoubtedly continue to restrict federal support of basic biomedical research and result in increasingly severe competition for the limited funds available. The time will come when even the best scientist cannot take continued funding for granted, and we must be prepared to provide some sort of salary guarantee to our senior scientists—and to those we want to attract—to keep them from going to universities offering tenure or to biotechnology firms promising very high salaries. To achieve this aim, we depend on far-sighted supporters who recognize the importance of basic biomedical research and appreciate how such research can thrive in the unusual scientific atmosphere that BBRI provides.

One of the most important assets of BBRI is its loyal friends, the members of its Corporation, and its Board of Trustees, whose material and intellectual support are the keystones to BBRI's success and on whom we can count to rise to the challenges of the future. On behalf of the staff, I should like to express our appreciation to these most important partners in our research enterprise.

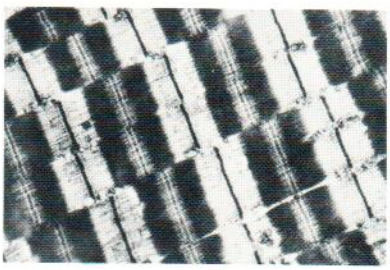


Henry Paulus, Ph.D.

Muscle—The Inside Story

A gymnast's leap, the beating of the heart, and the contraction of the uterus during childbirth—all are movements brought about by muscle contraction. While we may be aware of the muscles that move our limbs, we are perhaps less aware that the heart—the organ that keeps our blood circulating through our bodies and moves it through our lungs to replenish it with oxygen—is also a muscle. Even less familiar to us is "smooth muscle," a tissue so called because under a microscope it lacks the striated appearance of skeletal and heart muscle. Smooth muscle plays an important role in the functioning of such internal organs as the uterus, intestine, and blood vessels.

Dr. John Gergely, Director of the Department of Muscle Research.



Electron micrograph of a longitudinal section of a skeletal muscle fiber, showing the typical pattern of striations.

Close-up: Why study muscle?

In the forty years since it was discovered that one of the major protein constituents of muscle plays a role in contraction, modern research has looked for an understanding of the machinery of muscle at the molecular level. By mapping the spatial organization of the molecules comprising muscle tissue, scientists hope to understand how these molecules effect—and regulate—motion. At BBRI we investigate the molecular "nuts and bolts" of the muscle engine and its control.

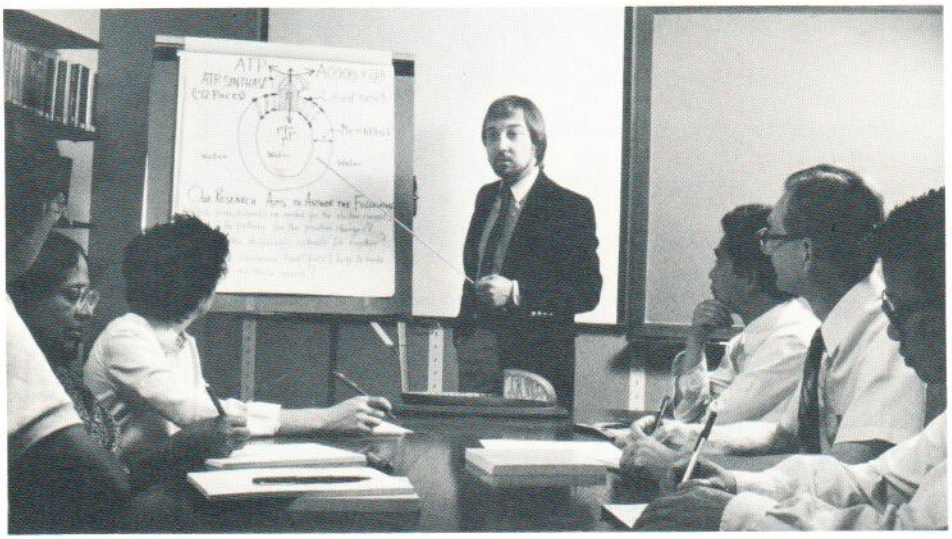
In the Department of Cell Physiology, researchers explore the production of ATP, the "fuel" for muscle contraction and virtually all other bodily functions. Because defective ATP production causes some types of neurological disorders and myopathy, this work has important medical implications.

In the Department of Muscle Research, the proteins that make up and regulate the muscle engine are examined at the submolecular level. Other studies explore the surrounding membrane of muscle and the calcium "pump," which controls the traffic of electrically charged calcium and so regulates muscle contraction. Finally, researchers are investigating the genetic blueprint of myosin, one of muscle's major protein constituents. This effort will help to illuminate the role of genes in muscle development in general, and specifically in the normal and abnormal heart.

Our growing knowledge of the fundamental components of muscle provides the scientific basis for understanding a number of diseases, from muscular dystrophy and cardiovascular disease to gastrointestinal disorders and complications of childbirth.

ATP: The Fuel of the Muscle Engine

Essential for many cell functions, ATP (**a**denosine **tri**phosphate) is composed of carbon, phosphorus, hydrogen, nitrogen and oxygen. Its production begins with the breakdown and oxidation of the food we eat and is completed mostly within "mini-cells" inside the animal cell. In these mini-cells, called mitochondria, the electrical energy generated by the oxidation of foodstuffs is converted into chemical energy stored in the form of ATP.



Dr. Michael Pringle discussing his research at a seminar.

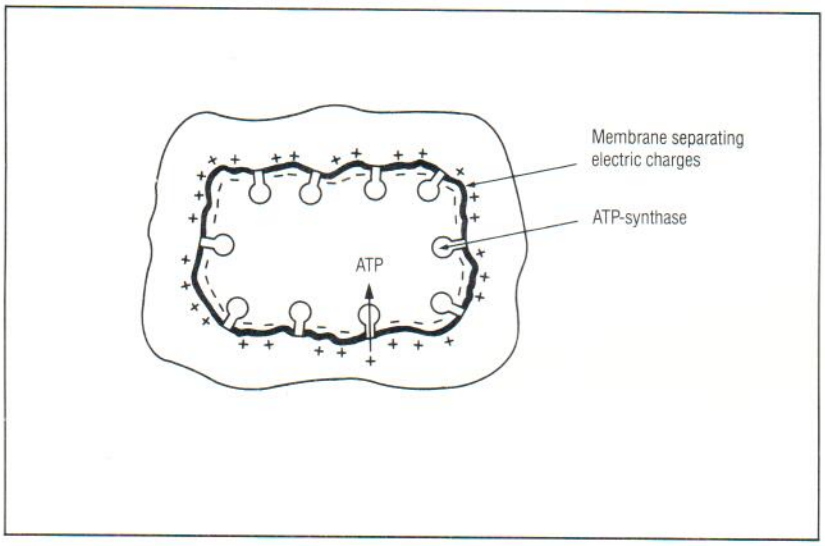
Close-up: The cell's ATP factories

A closer look at the mitochondria, the "factories" inside the cell, reveals an enzyme called ATP-synthase, located in small, lightbulb-shaped protrusions in a mitochondrion's membrane. This enzyme manufactures energy-rich ATP by harnessing the electrical energy produced by the oxidation of foodstuffs.

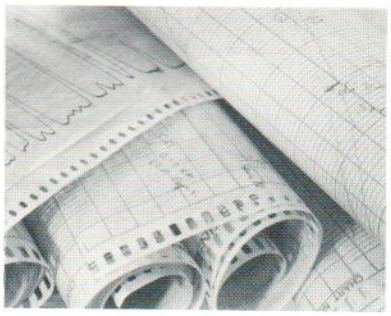
Dr. Michael Pringle explores the way in which ATP-synthase uses the movement of an electrical charge through a membrane to generate the chemical energy stored in ATP. He is looking for the crucial components of this system and their arrangement in the mitochondrion. ATP-synthase is actually a complex of twelve subunits, and he and other researchers are studying these in detail to determine the pathway of the electrical charge. Which of the subunits are necessary for its passage through the membrane? How do these subunits work together to facilitate that passage?

One way to study how electrical energy passes from the outside to the inside of the membrane is to inhibit the passage of the electrical charge through it and observe how various chemical groups within the membrane interact with the inhibiting agent. Through this and other methods, researchers are building up a picture of the components needed for passage of electrical charge through membranes.

The ATP is released into the cell proper, where its cleavage to yield phosphate provides the energy needed for various tasks. In muscle, breakdown of ATP produces the energy for contraction. Through an understanding of ATP production, we may be able to understand its role in some muscle diseases, especially those involving a defective ATP-synthesizing machinery.



Schematic representation of a mitochondrion and the arrangement of ATP-synthase.



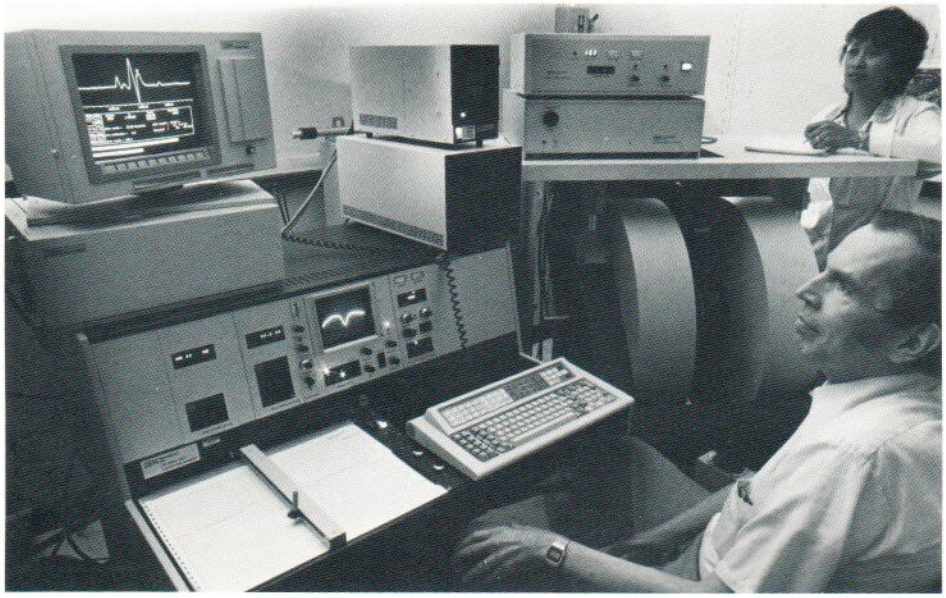
When experiments are done, evaluation of the experimental records still requires a major effort.

Lipids, fat molecules that are part of the membrane of mitochondria, play an important role in electrical energy transfer. By making artificial mitochondria from purified proteins and synthetic lipids similar to those found in natural cells, researchers are able to study the electrical properties of these so-called proteoliposomes. This simpler system avoids interference by other proteins or chemical reactions which occur in native mitochondria.

"ATP is the body's 'energy currency', essential for everything from the operation of heart muscle to the working of the nervous system," notes Dr. Pringle. "By building up a picture of the normal ATP production mechanism, we hope to understand the role of defects in that system in aging, obesity, and some muscle disorders. It may also help us to understand the sustained production of ATP necessary for some types of muscle."

How Muscles Contract

About forty years ago, the protein myosin was identified as a major constituent of the muscle contraction apparatus. Myosin molecules are long rod-like structures with two "heads." They make up the so-called "thick" filaments in muscle fiber and contribute to the striated appearance of heart and skeletal muscle seen under the microscope.



Dr. John Seidel studying the flexibility of the myosin molecule by electron spin resonance.

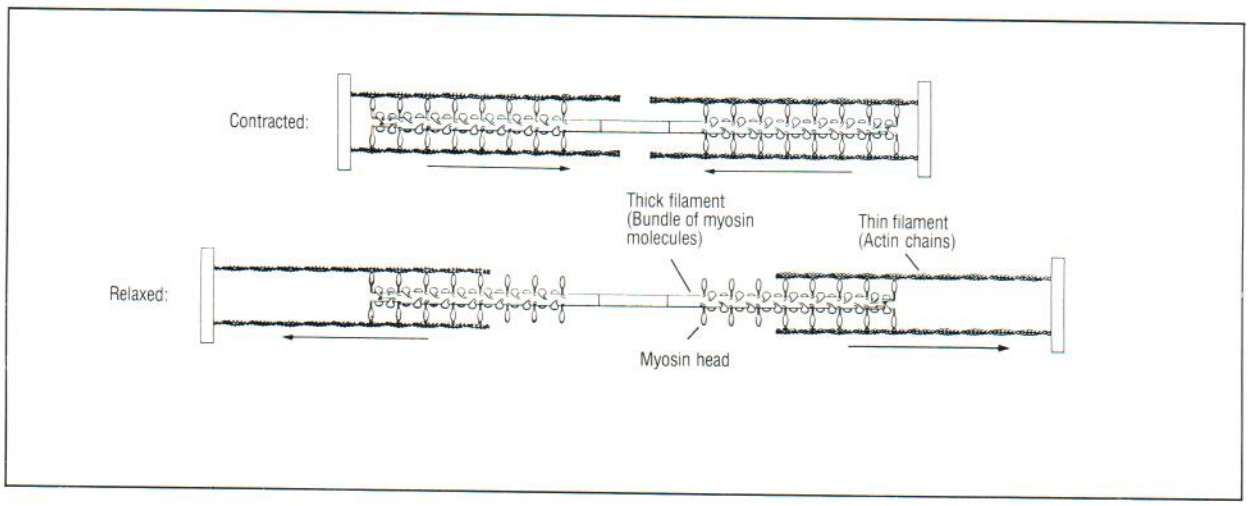
Close-up: Regulating contraction in smooth muscle

Both striated and smooth muscle contain the essential ingredients of contraction—actin, myosin and ATP. However, the regulatory processes in these muscles differ, and the ATP that fuels their contraction is activated by a different chemical.

In striated muscle, ATP breakdown is activated by electrically charged calcium (calcium ions) acting on the thin filaments of actin. In smooth muscle, the type responsible for contraction in many internal organs, calcium ions are involved only indirectly: they induce the transfer of phosphate to the myosin heads, where phosphate regulates the breakdown of ATP and, thus, contraction.

Dr. John Seidel investigates how the phosphate signal regulates the contraction of smooth muscle in blood vessels. He has found that the "neck" region of the myosin molecule plays a crucial role in phosphate's regulation of ATP breakdown in the myosin heads. He and other researchers have identified a number of sites in the neck and head regions of the molecule that are directly involved in transmitting the phosphate signal to the ATP-driven actin-myosin motor.

It is in the myosin "heads" that energy-rich ATP breaks down when myosin binds to the "thin" filaments of muscle, made primarily of the protein actin. The heads attach and detach at various places along the thin filaments. In this way, myosin moves along the actin filaments, like a boat propelled by several sets of oars dipping into and pushing against the water. Contraction occurs as the thick and thin filaments are pulled past one another.



Schematic diagram of a myofibril, in relaxed and contracted form. Movement is generated by the changing positions of the myosin heads on the actin filaments.

The techniques used in this work include enzymatically chopping a myosin molecule into discrete sections and observing, under the electron microscope, each region's response to chemical stimuli. These studies have been much aided by Dr. Renne Lu's chemical dissection of myosin.

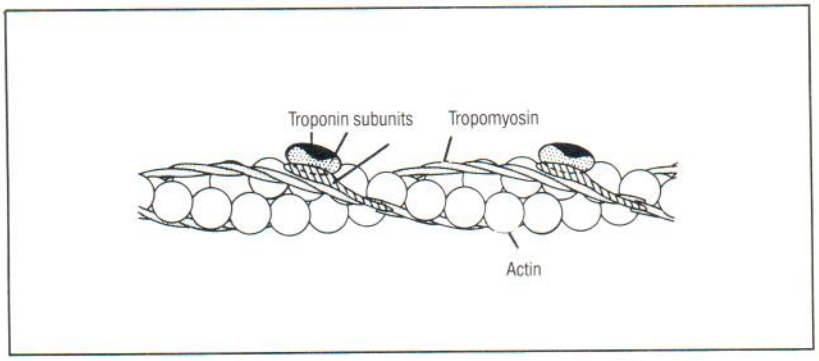
An important point, says Dr. Seidel, is the great flexibility of the myosin molecule. This flexibility provides new clues about the pathway of the phosphate signal from the neck of the molecule to the head, where ATP breakdown actually occurs.

Study of smooth muscle myosin will provide us with a better scientific understanding of how contraction is controlled in important internal organs like the uterus and intestine. Investigations of contraction regulation in arterial smooth muscle may help us to understand how smooth muscle in the arteries regulates blood pressure.

Regulation in Striated Muscle

In striated muscle, contraction is regulated through an additional set of proteins arranged at intervals along the backbone of actin, the thin filament. By stripping actin of these regulatory proteins, called troponin and tropomyosin, scientists have learned that without them, the process of contraction would continue uncontrolled until all the ATP was used up. We now know that in striated muscle, troponin and tropomyosin serve as two components of a switch, operated by calcium ions, which regulates the interaction of myosin, actin and ATP.

Dr. Sherwin Lehrer reviewing experimental results on tropomyosin for presentation at a meeting.



Schematic arrangement of the regulatory proteins tropomyosin and troponin along the actin filament.

Close-up: Mapping the interior

The regulatory apparatus of troponin and tropomyosin in striated muscle is activated by small amounts of calcium ions. These are released from a membrane capsule within the muscle cell, as discussed in the next section.

Dr. Paul Leavis, along with other researchers in the Muscle Department, is working to build a molecular-scale picture of troponin. It is in one of this protein's three subunits that calcium binding takes place. During its interaction with calcium ions, the subunit's structure changes, communicating the "stop" or "go" message, first to the other two troponin subunits and then to tropomyosin and actin.

Investigations of these structural changes involve separating troponin into its three subunits and attaching fluorescent substances to various locations in each. The properties of light emitted by such fluorescent "tags" reflect the chemical groups that surround them.

When calcium ions are added to the calcium-binding subunit, the fluorescent tag "reports" the changes in the configuration of the protein. This gives researchers clues to what must happen to the subunit's structure in order for calcium to communicate its message to the next subunit and on to tropomyosin and actin.

Researchers in the Muscle Department are working to describe the processes and structural changes by which these proteins regulate muscle contraction. Using a variety of methods, they map the interiors of these proteins and gauge the changes that occur in their structures during the regulatory process.

Dr. Paul Leavis setting out to measure the effect of calcium on the fluorescence of troponin.

Fluorescent probes can also be used as "molecular rulers" to measure distances within a subunit and between subunits and other proteins. Light signals can be transmitted between appropriately chosen probes, and the efficiency of transmission differs according to the distance between them. This makes it possible to measure the shifts in protein configuration that are provoked by calcium ions.

Dr. Sherwin Lehrer and coworkers are working with fluorescent probes and other methods to map the interior of the tropomyosin, the other component of the "switch" mechanism. They examine the changes tropomyosin undergoes in order to communicate to actin the signal it receives from troponin.

Their goal is to test whether, as is currently believed by some scientists, tropomyosin moves aside to admit or prevent the interaction of myosin with actin, or whether, as others believe, a more subtle change in tropomyosin induces a further change in actin. Such use of fluorescent probes in the study of tropomyosin may make it possible to construct a more realistic molecular model for the structure of tropomyosin and its role in regulation.

Muscle's Calcium Reservoir and Pump

Muscle contraction is triggered by a nerve impulse, which travels along the muscle cell membrane and its extensions—the "transverse tubules"—penetrating into the interior of the muscle fiber.

Drs. Noriaki Ikemoto and John Gergely discussing the relationship of sarcoplasmic reticulum to the contractile filaments of muscle.

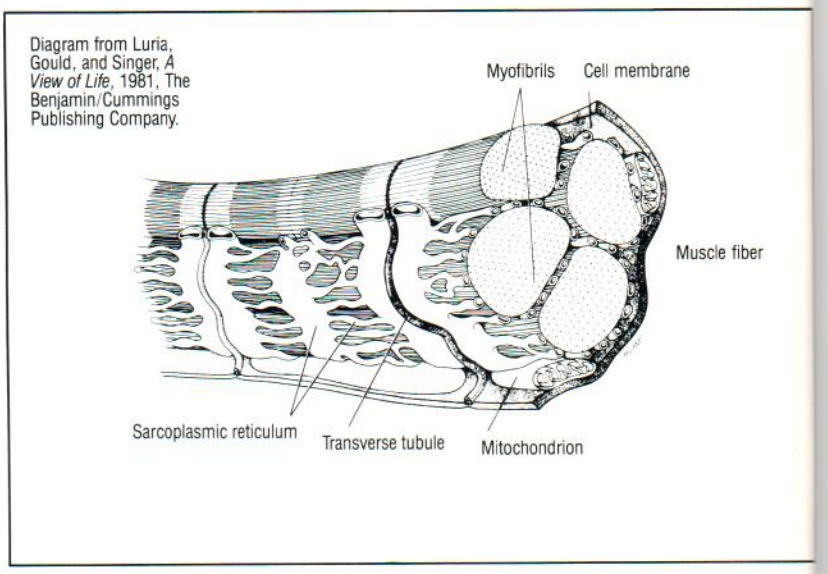


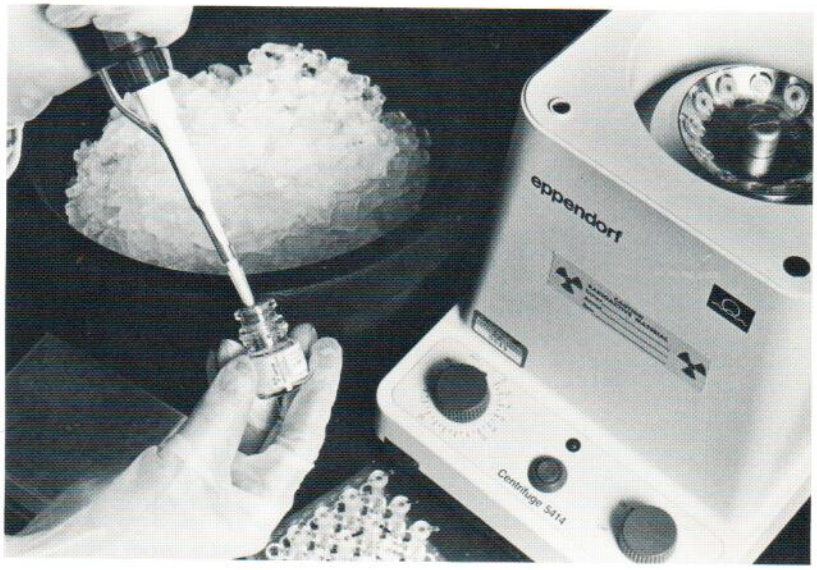
Diagram of muscle fibers with sarcoplasmic reticulum and transverse tubules.

Close-up: The dual job of the sarcoplasmic reticulum

A central research question revolves around the dual role of the sarcoplasmic reticulum—its release of calcium ions into the muscle cell to start a contraction and its ability to draw calcium ions back into this reservoir to produce relaxation. The latter process, fairly well understood, is controlled by an ATP-fueled pump, which consists of a specific protein built into the sarcoplasmic reticulum. When the pump is activated by an increase of calcium ions in the muscle cell, it brings calcium ions back into the reservoir, thereby lowering the calcium concentration around the muscle filaments and putting the muscle to rest. The cell is now ready for the next nerve impulse to trigger a contraction.

Less understood, however, is the process by which the nerve impulse is transmitted via the transverse tubules to the sarcoplasmic reticulum, triggering the release of calcium to the muscle filaments. In an effort to elucidate this elusive process, Dr. Noriaki Ikemoto and his colleagues have isolated a segment of transverse tubule with a portion of the adjacent sarcoplasmic reticulum. Through studies of this preparation, the group hopes to chart the route of the nerve impulse from transverse tubule to sarcoplasmic reticulum.

By a process not yet fully understood, the impulse travels within the cell along the transverse tubules and reaches the sarcoplasmic reticulum, a membrane capsule containing calcium ions. There the impulse triggers a flood of calcium ions through the membrane to elicit muscle contraction by interaction with the appropriate proteins. The entire process, from impulse to contraction, takes about one one-hundreth of a second.



A muscle protein being tagged with radioactivity.

The nerve impulse can be mimicked by changing the ions in the surrounding medium. This allows investigation of the process by which a nerve impulse activates muscle and of the components involved.

One experimental approach uses antibodies. Antibodies that strongly bind to specific muscle proteins can be prepared by immunizing animals with the appropriate purified protein. When such antibodies are added to an isolated preparation of transverse tubules and adjacent sarcoplasmic reticulum, the antibodies will combine with specific proteins and inhibit their function. By examining ensuing changes in calcium release, it is possible to identify the proteins needed in the process.

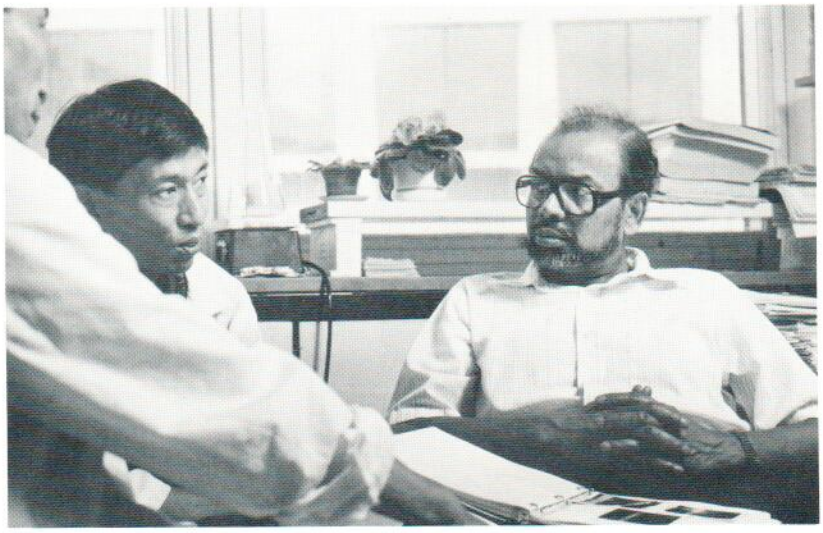
Another approach is pharmacological, employing a variety of drugs that inhibit the transmission of the nerve impulse to the sarcoplasmic reticulum in the preparation. Yet another method involves tagging the components involved with radioactive isotopes in order to map out the molecular pathway of the process.

Through these methods the researchers can either inhibit the release of calcium or artificially stimulate it. Such experiments make it possible to identify key events. Kinetic studies even permit measuring the time it takes to release calcium.

The next step, notes Dr. Ikemoto, will be to use some of these techniques to determine where exactly the molecular components of the calcium pump are positioned in the membranes.

Genes: The Blueprints for Muscle Proteins

An important question in muscle research concerns the actual production, or biosynthesis, of the proteins making up the muscle engine. Each of the proteins discussed in these pages exists in many forms and is controlled by a family of genes. These genes provide a code for the assembly of a protein from amino acids. Different members of the gene families are active at various times in the development from embryo to adult, as well as during adaptation to new functional demands.



Dr. Satyapriya Sarkar and colleagues discussing the electrophoretic separation of enzyme-digested DNA.

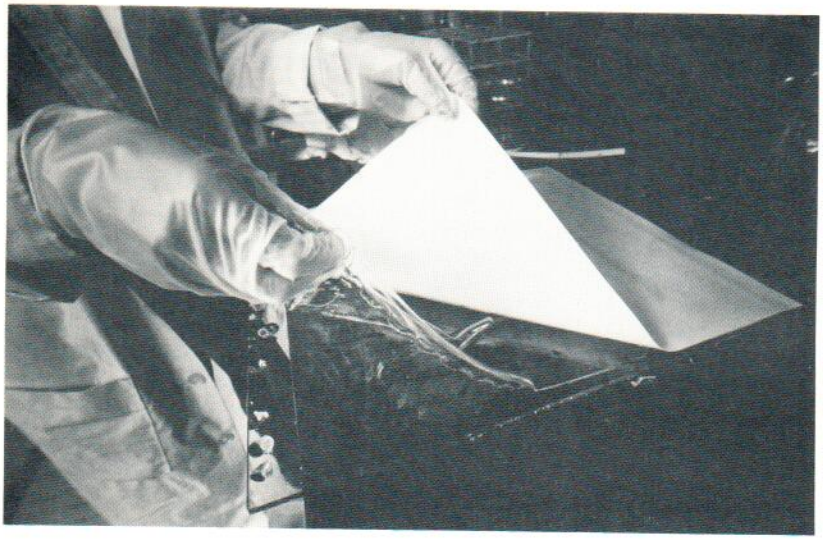
Close-up: How genes control myosin function

Myosin, one of the major muscle proteins, is a paradigm for the study of gene activity because of the flexible response of its genes to various influences. The molecular structure of myosin is altered by physiological and pathological factors such as development after birth, heart overload, exercise, and hormonal changes.

These changes, at the molecular level, are caused by the "switching on and off" of some of the genes. The "switching," like a complicated set of traffic lights, accounts for the variation of myosin from animal to animal, between various tissues in the body, and from embryonic to fully developed muscle. It also accounts for the response to hormonal, neural, and other factors.

Dr. Satyapriya Sarkar has focused his research on the adaptive changes of myosin. One investigation, in collaboration with Drs. Sreter and Gergely, involves the study of the myosin genes' sensitivity to exercise and nerve stimulation in so-called "fast" and "slow" muscle. Fast muscle is responsible for the sprinter's rapid, short-lived contraction, while slow muscle develops in the long-distance runner, producing slower but more sustained contraction. In response to the use to which the

Using techniques of molecular genetics, researchers are investigating how genes program these developmental changes. Also under investigation are the various forms of muscle proteins which occur in functionally different muscle tissues.



DNA labeled with radioactive phosphorus is transferred from the gel to the paper.

Reading a DNA sequence from a film of a sequencing gel.

muscle is put, the traffic-light pattern of the myosin genes switches to accommodate the new command, and the structure of myosin changes.

Dr. Sarkar is also isolating and characterizing genes in an effort to determine whether there are regulatory sequences within that gene or near it which influence how and when that particular gene will be switched on. In particular, he is studying the genetic makeup of myosin in the normal and in the diseased heart. His work builds on Drs. Sreter's and Mabuchi's finding that the distribution pattern of various forms of myosin changes in disease. Using genetic engineering techniques, Dr. Sarkar is now trying to determine whether the regulatory influence on some genes changes during cardiomyopathy. Using DNA probes, he and other researchers measure the extent to which a particular gene is activated.

By studying the genetic machinery of muscle, and in particular, that of myosin, scientists in the Muscle Department hope to gain a better understanding of various human heart diseases, as well as the role of aging, exercise and other factors in the development of muscle tissue.

Thank You!

The generosity of far-sighted foundations, individuals, and businesses this year provided $175,775 for basic medical research at BBRI. Each gift contributes to the excellence which is the hallmark of BBRI's research. Each donor is a valued partner in BBRI's work.

At a reception—Mrs. Elmer O. Cappers and Mr. Cappers, guests, with Dr. Peter Davison, Director, Department of Fine Structure

At a reception—Dr. Shan-Jiong Shen, Distinguished Visiting Scientist, with Mrs. Robert U. Ingalls and Mr. Ingalls, guests, and William B. Tyler, Chairman

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Dr. D. Rao Sanadi, Director, Department of Cell Physiology, with (background) Dr. Henry Paulus, Executive Director and Director, Department of Metabolic Regulation; (foreground) Peter B. Sholley and John F. Taplin, Trustees; and Dr. John Gergely, Director, Department of Muscle Research

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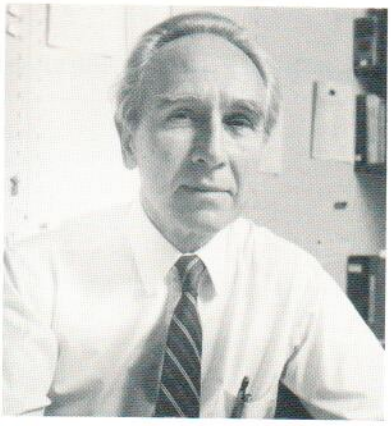

Dr. Peter F. Davison, Deputy Executive Director and Director, Department of Fine Structure Research

BOSTON BIOMEDICAL RESEARCH INSTITUTE
BALANCE SHEETS
AUGUST 31, 1986 AND 1985

	1986	1985
ASSETS		
CURRENT ASSETS		
Cash	$ 1,079,087	$ 506,680
Grants receivable	4,441,264	4,605,476
Pledges receivable	37,300	32,352
Prepayments, deposits and other receivables (note 6)	183,233	141,269
Investments, at market value (cost 1986—$2,355,204 1985—$2,121,810) (note 5)	2,928,113	2,295,756
Total current assets	8,668,997	7,581,533
FIXED ASSETS: (notes 1 and 2)		
Leasehold improvements	1,935,632	1,935,632
Research equipment	3,567,053	3,329,969
Furniture and fixtures	48,799	47,129
Total	5,551,484	5,312,730
Less accumulated depreciation and amortization	3,644,678	3,410,411
	1,906,806	1,902,319
	$10,575,803	$9,483,852
LIABILITIES AND FUND BALANCES		
CURRENT LIABILITIES		
Accounts payable and accrued expenses	$ 40,576	$ 40,000
Overhead and fringe benefit adjustment payable	579,410	417,988
Deferred grant income (note 4)	4,762,971	4,650,251
Deferred fund (building) (note 4)	115,702	115,702
Total current liabilities	5,498,659	5,223,941
FUND BALANCES (note 1)		
Operating	747,075	495,306
Plant and equipment	1,977,234	1,501,682
Permanent research	446,029	360,604
Fixed assets (notes 1 and 2)	1,906,806	1,902,319
Total fund balances	5,077,144	4,259,911
	$10,575,803	$9,483,852

See accompanying notes to financial statements.

BOSTON BIOMEDICAL RESEARCH INSTITUTE
STATEMENTS OF REVENUES, EXPENSES AND CHANGES IN FUND BALANCES
FOR THE YEARS ENDED AUGUST 31, 1986 AND 1985

	1986	1985
REVENUES		
Grants	$5,356,104	$4,777,605
Equipment replacement	93,892	98,850
Contributions and pledges	175,775	153,129
Property and equipment purchased (notes 1 and 2)	238,754	226,259
Investment income	611,069	279,007
Total	6,475,594	5,534,850
EXPENSES (by department)		
Muscle Research	2,536,970	2,240,021
Cell Physiology	1,227,757	1,161,248
Fine Structure	521,623	458,045
Metabolic Regulation	881,385	777,387
General Research	199,085	118,915
Fund Raising	38,854	40,149
Purchase of fixed assets (note 1)	18,420	14,088
Depreciation and amortization (note 2)	234,267	380,281
Total	5,658,361	5,190,134
NET ADDITION TO FUNDS	817,233	344,716
FUND BALANCES, BEGINNING OF YEAR (note 1)	4,259,911	3,915,195
FUND BALANCES, END OF YEAR (note 1)	$5,077,144	$4,259,911

See accompanying notes to financial statements.

BOSTON BIOMEDICAL RESEARCH INSTITUTE
NOTES TO FINANCIAL STATEMENTS
AUGUST 31, 1986 AND 1985

(1) – 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. These funds are deemed to be earned and reported as revenues when the Institute has incurred expenditures in compliance with the specific restrictions. Amounts received but not yet earned are reported as restricted deferred amounts (See note 4).

*Fixed assets fund represents 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 $93,892 in 1986 and $98,850 in 1985. In addition, $18,420 of equipment was charged to the operating fund in the year ended August 31, 1986, $14,088 in 1985 and added to the plant fund.

(2) – Plant Assets and Depreciation:

The 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 the 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 ten year useful life of the assets. All depreciation and amortization is charged to the plant fund.

(3) – Government Grants:

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

(4) – Changes in Deferred Restricted Amounts:

	1986			1985
	Building Fund	Grants & Contracts	Total	Total
Balance, beginning of year	$115,702	$ 4,650,251	$ 4,765,953	$4,023,892
Additions:				
New grants awarded		5,380,976	5,380,976	5,442,509
Contributions and pledges		1,541	1,541	1,000
Investment income	27,556	77,848	105,404	49,476
	143,258	10,110,616	10,253,874	9,516,877
Deductions:				
Funds expended for designated purposes		5,347,645	5,347,645	4,735,580
Transfer of investment income from Building fund	27,556		27,556	15,344
Balance, end of the year	$115,702	$ 4,762,971	$ 4,878,673	$4,765,953

(5) – Investments:

Investments consist of corporate and government bonds and listed stocks. Also included is an $800 investment made in 1982 in Boston Biotechnology Corporation. This company was formed to utilize and commercialize certain technical processes originated at Boston Biomedical Research Institute and elsewhere.

The investment holding represents the entire outstanding stock of Boston Biotechnology Corporation and is shown at cost since Boston Biotechnology was inactive through the Institute's year end.

(6) – Advances to Subsidiary:

The Institute has advanced $109,779 to Boston Biotechnology Corporation. This amount is included in the category Prepayments, deposits and other receivables.

Board of Trustees
Boston Biomedical Research Institute
Boston, Massachusetts

I have examined the balance sheets of Boston Biomedical Research Institute as of August 31, 1986 and 1985, and the related statements of revenues, expenses and changes in fund balances for the years then ended. My examinations were made in accordance with generally accepted auditing standards and accordingly included such tests of the accounting records and such other auditing procedures as I considered necessary in the circumstances.

In my opinion, the aforementioned financial statements present fairly the financial position of Boston Biomedical Research Institute as of August 31, 1986 and 1985, and the results of its operations and changes in fund balances for the years then ended, in conformity with generally accepted accounting principles applied on a consistent basis.

John Vecchi/Certified Public Accountant
124 Crescent Road, Needham, Massachusetts 02194
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October 1, 1986

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