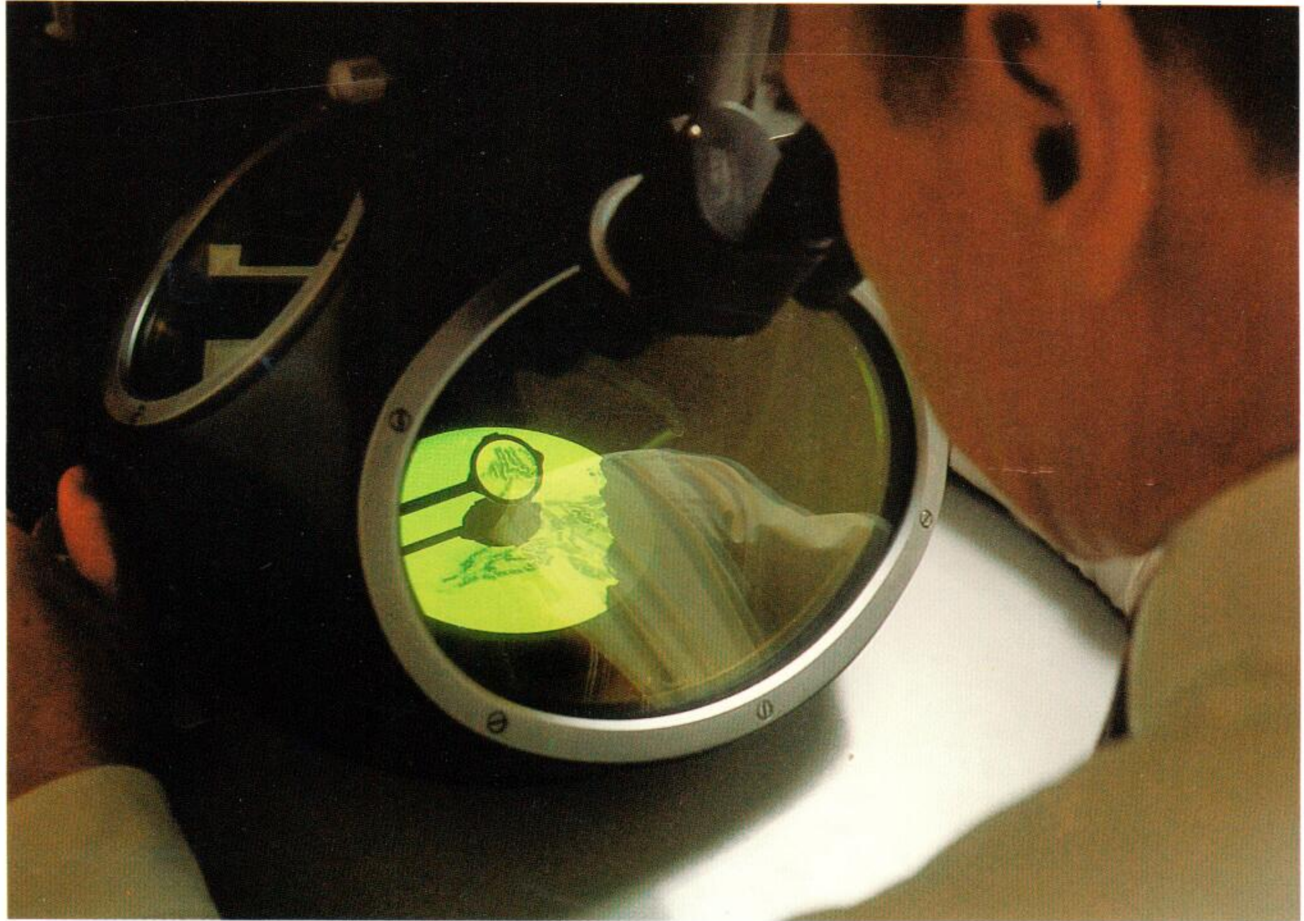
BOSTON BIOMEDICAL RESEARCH INSTITUTE

1987 ANNUAL REPORT



"Although biomedical researchers study various ways to treat disorders, the goal is to find cures—and what is even better, ways to prevent disease. To do this, they must first understand the disease—not just what its symptoms are and what it usually does to the patient, but exactly what has happened inside the body to cause those symptoms and those consequences. In short, researchers must find out what is happening at the cellular and molecular levels."

—Brochure on the occasion of the NIH Centennial (1987)

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 almost two decades 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.

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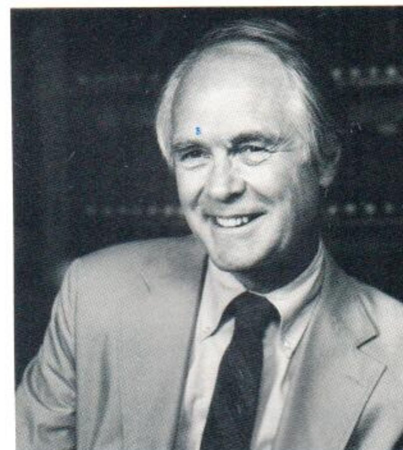
Report of the President



This past year has been another one of solid achievement for the Institute. The staff, under the able leadership of the Department Directors, have continued to produce excellent work. Basic research on questions such as how living cells and their molecules work and interact often appears unspectacular. Yet it is this type of research, which takes place at BBRI and other basic research facilities, that produces links in our chain of knowledge from which the occasional spectacular results are achieved. We are proud of the role our staff plays in advancing knowledge in these vital areas. As one manifestation of the regard in which our staff is held in the worldwide scientific community, I am pleased to report that Dr. John Gergely received an honorary doctorate from Semmelweis University Medical School in Budapest, Hungary, this spring.

This year has seen BBRI enter into two sponsored research contracts. One of these is funding Dr. Suh-Der Tsen's work in evolutionary biochemistry, which aims to tailor enzymes for specific uses. The other funding relates to Dr. John Codington's research on carcinoma detection, which seeks to develop antibodies for use in a blood test for certain kinds of cancer. This is a welcome supplement to our NIH and NSF grants, and we are pleased to have the opportunity to work with private funding sources.

This year has also seen BBRI establish a new record in annual giving, passing our ambitious \$180,000 goal and reaching \$196,540. We are most appreciative of the effort this represents by our Development Committee, particularly its chairman, Peter Sholley, who is relinquishing his post this year with much deserved credit for the magnificent results he has achieved.

The continued support from individuals, corporations and foundations to our annual appeal is most gratifying, and we are proud that it reflects the confidence BBRI enjoys in the Boston community. We are particularly pleased to have received a number of first-time gifts from foundations this year—most significantly the Amelia Peabody Foundation. We also received this year what I hope will be the first of many endowment gifts. Finally, I would like to note the establishment of the Elizabeth Slayter Memorial Cancer Research Fund by her husband, Dr. Henry Slayter. We are deeply grateful to him for choosing this way of remembering his wife, who was an eminent biologist and writer. This fund will be used to aid Dr. Codington's research.

Two staunch supporters have retired from their pro bono positions with BBRI this year. Denholm Jacobs, one of the founding Trustees of the Institute, stepped down from his position as Trustee but remains a member of the Corporation. Wesley Dixon retired as a member of the Corporation. They should know they leave with the thanks and appreciation of the entire BBRI family for their efforts on behalf of the Institute.

John B. French

John B. French

Report of the Executive Director

This annual report follows last year's pattern of featuring the contributions of BBRI scientists to a single research area. The field we have selected this year is the study of the membranes which separate all cells from their surroundings and subdivide their interiors. In spite of their universality, cell membranes have many functions, and the research programs that the report describes not only give you a glimpse into a very important area of cell biology but illustrate the diversity of interests and experimental approaches of BBRI scientists. A point worth noting is that the membrane research described here is done in all four of BBRI's departments. It is the diversity of interests in the absence of preconceived research boundaries that makes the research atmosphere at BBRI so stimulating and exciting.

During the past year, BBRI has maintained its momentum as an outstanding research institution. In spite of the fact that nearly all research grants awarded by NIH suffered across-the-board cuts, the total grant support we received increased by 6%. BBRI scientists published more than 40 scientific papers in major journals and were invited as guest speakers at numerous international conferences, ranging as far afield as India and China.

It is with mixed feelings that I report the resignation of a valued colleague, Dr. Satyapriya Sarkar. For almost 20 years Dr. Sarkar was a member of the Department of Muscle Research, where he pioneered the application of molecular genetic approaches to the study of muscle proteins. He has accepted a tenured professorial position at Tufts University, and we wish him continued success in his scientific endeavors. I should add that we have not lost Dr. Sarkar entirely, for he retains an appointment as Visiting Scientist at BBRI, and we are looking forward to continued scientific collaboration.

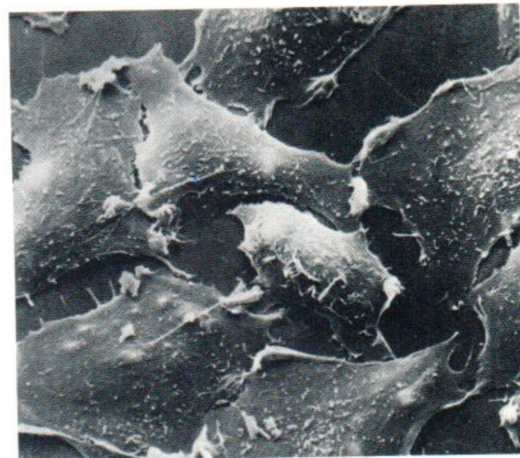
The resignation of a senior member of our faculty to accept a tenured position at another institution brings home the importance of an institution's ability to offer salary guarantees to senior scientists. At this time, BBRI lacks the financial resources needed both to maintain an adequate operating reserve and to underwrite faculty salaries. The accumulation of an endowment for this latter purpose should be a top priority. Only by offering a salary guarantee, even a limited one, to our senior scientists can we hope to retain the best of our present staff and at the same time attract top-flight new scientists to replace senior faculty who have reached retirement age. I see this as one of the greatest challenges to our future, but I am confident that our loyal supporters—trustees and members of the Corporation, foundations and other friends—will help us meet this challenge in the years ahead.

In closing, let me thank our good friends, who are acknowledged elsewhere in this report, for participating in our quest for a better understanding of the fundamental life processes by so generously donating their money, time, and wisdom. Their enthusiasm and confidence in the importance of basic biomedical research are a great source of encouragement to our scientists.

Henry Paulus, Ph.D.

GOOD FENCES MAKE GOOD NEIGHBORS

A cell in the body can be likened to a country in the community of nations. It is to a certain degree self-sufficient but thrives through commerce with its neighbors. To reconcile the conflicting requirements of independence and interdependence, a country establishes borders and mechanisms that control the flow of goods across these borders according to its needs and the information it receives from abroad.



Photomicrograph of normal hamster cells. The outside of each cell is its membrane.

The borders of a cell are the membranes which surround it like an envelope and even subdivide its interior into several compartments as a country is divided into provinces. The very essence of an organism lies in how each of its cells responds to its environment, a response which is defined by its membranes. Indeed, most disease results from inappropriate cellular responses or from assaults on the cell membrane by invaders such as viruses and toxins. The study of how the molecules that make up the membranes are assembled, of how the flow of substances across the membrane boundaries is controlled, and of how information is sent across membranes into the cell is one of the most exciting and challenging areas of biochemistry and cell biology. It is only now attaining maturity, yet the answers it is providing are of crucial importance to our understanding of the most basic aspects of cell function.

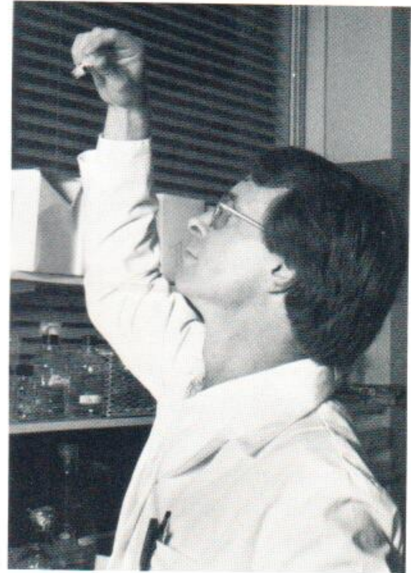
At BBRI, we study many different aspects of membrane function. Researchers in the Department of Cell Physiology explore the transport of nutrients across the cell membranes and the detailed mechanism of how the energy released by the combustion of foodstuffs is harnessed to drive cellular functions. In the Department of Metabolic Regulation, the question of how certain proteins are marked for export and then secreted by the cell is being investigated. Scientists in the Department of Muscle Research study how the transmission of a nerve impulse to muscle triggers the passage of calcium across the cell membrane and yet other membranes within the cell to cause muscle contraction. Finally, studies in the Department of Fine Structure focus on how cells can shield themselves against attack by the immune system and how this defense might be thwarted in a way that allows the selective destruction of tumor cells.

FRONTIERS

WHAT ARE BIOLOGICAL MEMBRANES?

Since the cell is surrounded by water and its contents are essentially aqueous, its membrane envelope necessarily consists of material that will not mix with water, namely fatty molecules such as lecithin that are called lipids. Lecithin is a *phospho*lipid, with one portion containing phosphorus, which is *hydrophilic* (i.e. likes water), and another portion containing fat, which is *hydrophobic* (i.e. repels water). When dispersed in water, the lecithin molecules align into sheets which in turn pair to form so-called *bilayers*, with the hydrophilic groups on the surfaces in contact with water and the hydrophobic groups in the interior. The hydrophobic interior of the bilayers makes them impermeable to water and thus an effective barrier to most water-soluble compounds, such as sugars and other nutrients, sodium, calcium, phosphate, and so on.

However, membranes are not composed solely of phospholipids but also contain a variety of proteins that are embedded in the membrane bilayer. Even though each protein may represent only a very small fraction of the membrane's mass, it is these proteins which carry out the membrane's functions and are thus its key constituents. Because different membranes may have diverse functions, their protein composition is often quite different, and researchers study different membranes depending on the problem they wish to investigate. In the pages that follow, we describe research at BBRI that focusses on the structure, mode of action, and control of a variety of membrane proteins with the aim of achieving a basic understanding of how membranes work.



Dr. Terrence Scott cloning the gene of a membrane protein in the colon bacillus.

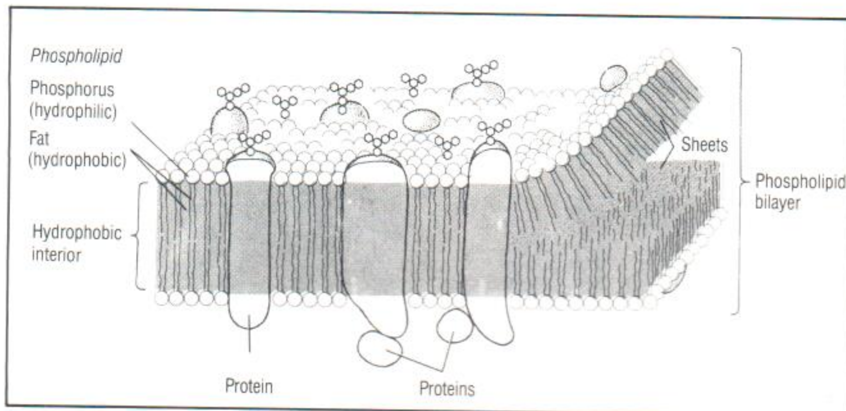


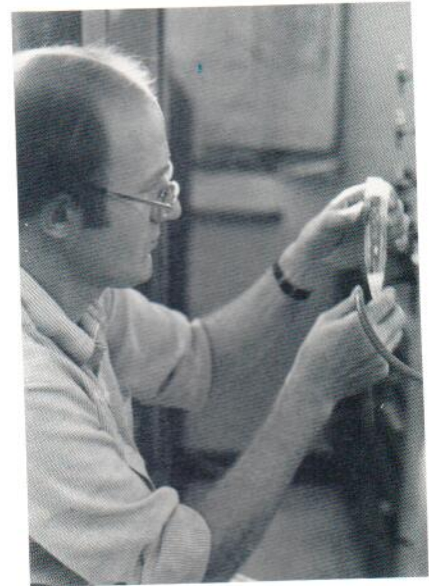
Diagram of the structure of a membrane showing the phospholipid bilayer and membrane proteins.

IMPORT/EXPORT

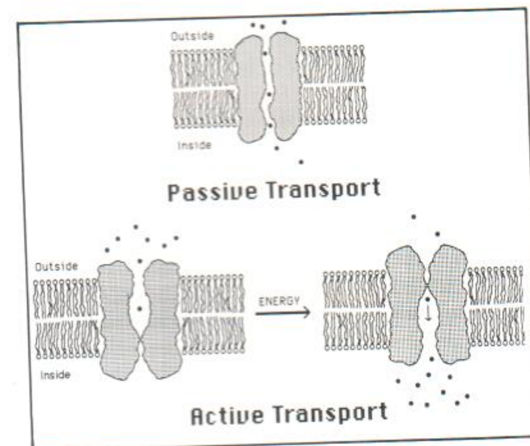
HOW IS SELECTIVE TRANSPORT ACROSS MEMBRANES ACCOMPLISHED?

Water soluble substances cannot ordinarily penetrate the membrane lipid bilayer, and their transport into the cell therefore requires the help of proteins. For each transport reaction, a particular protein or even a group of cooperating proteins is needed. There are two different kinds of transport reaction. One is the spontaneous movement from a region where a substance is in high concentration, and this is called *passive transport*. In this type of transport, a membrane protein somehow provides a channel through which the substance can diffuse from one side of the membrane to the other. The second kind of transport involves movement from a lower to a higher concentration and is called *active transport*. Active transport requires energy from a chemical reaction and involves proteins which are called pumps. How this energy actually drives the pump, which picks up one molecule at a time and moves it, is one of the most challenging problems in membrane research.

Phosphate is needed by all cells. Its transport across membranes is of special importance in the mitochondria, which use it to synthesize ATP from ADP as will be described in a later section. Dr. Hartmut Wohlrab has isolated the protein that transports phosphate across the mitochondrial membrane and is now attempting to characterize the part of the protein molecule that is concerned with the binding of phosphate and its transport. He does this by using chemical compounds that mimic phosphate but—unlike phosphate—form a chemical bond with the protein, thus tagging the parts involved in phosphate binding and allowing their identification. A fragment of the protein that contains the phosphate binding region has been isolated, and the study of its structure will provide important information on the mechanism of the binding and transport of phosphate into the mitochondria.



Dr. Hartmut Wohlrab with a sample of isolated phosphate transport protein.



Schematic representation of how proteins embedded in the lipid bilayer provide passive and active transport.

CUSTOMS AND IMMIGRATION

HOW IS TRANSPORT CONTROLLED?

In order for the cell to function properly, the concentration of its constituent molecules must be controlled and often maintained against a gradient. For example, the potassium ion (K^+) concentration is usually higher inside the cell than in the surrounding body fluids, and just the opposite is true for sodium ion (Na^+). How are the concentration differences maintained and controlled? In part, this is achieved by the membrane proteins acting as highly specific pumps. An additional mechanism involves so-called "gates" that open and close in less than one-thousandth of a second to regulate the flow through channels in the membrane. Signals such as hormones, nerve transmitters, calcium, and electrical potential trigger the opening of the gates. The actual opening and closing of the channels is believed to involve subtle changes in the shape of the membrane proteins.

Dr. Jen-Shiang Hong entering the nucleotide sequence of the gene of a transport protein into his computer.

On a longer time scale, membrane transport is controlled by changes in the amount of specific membrane proteins that are "induced" by the substances to be transported. Induction involves switching on the synthesis of new transport proteins and is especially common in microorganisms. Dr. Jen-Shiang Hong is studying how the presence of a sugar metabolite, phosphoglycerate, on the outside of a bacterial cell signals the turning on of the machinery for the synthesis of the phosphoglycerate transport protein inside the cell. He is approaching this problem by genetic techniques, studying the genes involved in phosphoglycerate transport and determining their nucleotide sequence. Dr. Hong's group has been able to identify three genes required for the sensing of phosphoglycerate and the transmission of the signals for the synthesis of the transport protein, suggesting a very complex regulatory mechanism. Their goal is to unravel the mechanism of action of these proteins in bacteria as a model for similar studies on human genes.

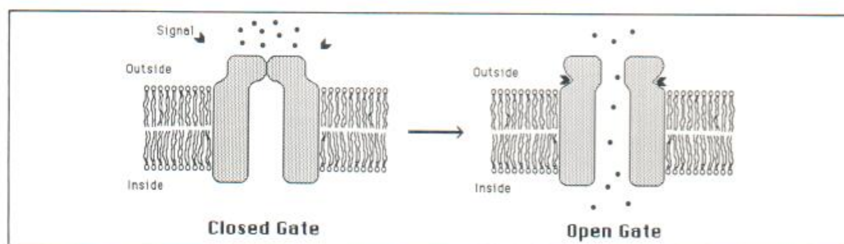
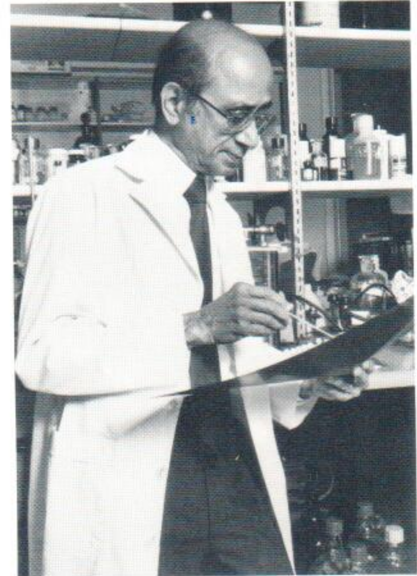


Diagram of how a "gate" controls the flow of ions through a membrane.

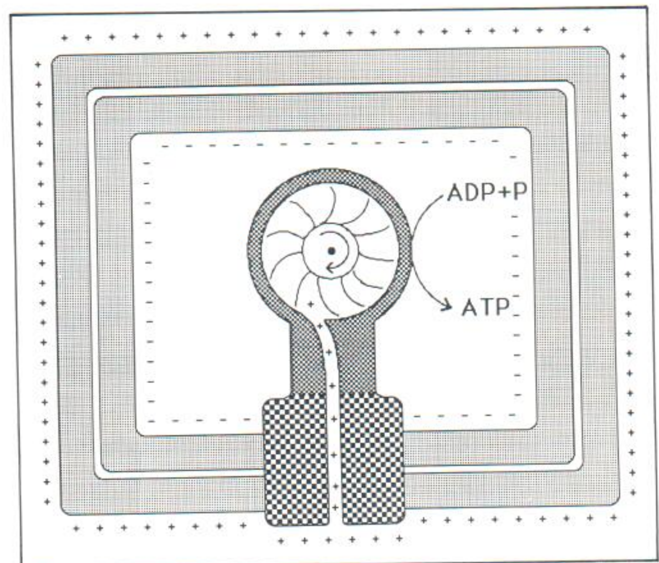
CURRENCY EXCHANGE

HOW MEMBRANES HARNESS METABOLIC ENERGY

A major question in biology is how the energy released by the chemical breakdown of food inside the cell can be utilized by the cell for its activities and growth. We know now that membranes play a key role in the synthesis of ATP (adenosine triphosphate), the energy currency of the cell that can be used for virtually all vital processes. Within all mammalian cells there are many small bodies called mitochondria, where ATP is made. It is in the mitochondria that food is ultimately degraded to carbon dioxide and water in a process that drives protons (positive charges) out of the interior of the mitochondria, leaving their interior negatively charged. The mitochondrial membrane is a good insulator and holds the charge like a microbattery until ATP is needed for the cell's activities—for example for muscle contraction, nerve conduction, or cell division. Then a channel for protons is opened, the protons reenter the mitochondrion and somehow promote the synthesis of ATP from ADP and phosphate. Essentially, the electrical energy of the "microbattery" is thereby converted to the chemical energy stored in ATP. This complex process is carried out by a highly organized assembly of enzymes known as ATP synthase, anchored in the mitochondrial membrane and composed of over 10 different proteins. Five or more of these proteins, called F_0, are actually embedded in the membrane bilayer and are organized into a proton channel. The other five, the so-called F_1 segment, are attached to F_0 but extend out of the membrane and contain the site at which ADP and phosphate are linked to form ATP.



Dr. Rao Sanadi studying the results of cloning one of the ATP synthase genes.



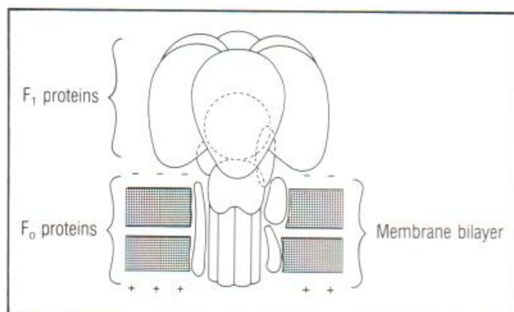
Schematic representation of how ATP synthase embedded in the inner mitochondrial membrane uses the flow of protons for the synthesis of ATP.

Dr. Saroj Joshi is engaged in mapping the arrangement of the protein subunits in ATP synthase and their topography in the membrane. She uses reagents with two reactive groups at either end of a variable spacer—a kind of chemical ruler—to crosslink the proteins in the complex. By identifying the proteins that are crosslinked with reagents that have spacers of different length, it is possible to deduce the distances between various pairs of subunits. Another approach involves the use of enzymes that digest proteins unless they are shielded by a lipid bilayer. This technique provides information on which parts of the subunits are actually embedded in the mitochondrial membrane.

Dr. Saroj Joshi using a pH meter to measure the concentration of protons.

Another investigation involves factor B, a protein which Dr. Rao Sanadi identified several years ago. He and Dr. Yuguo Huang have now found that factor B is actually part of the F_o proton channel, which is especially exciting since much progress has already been made in the elucidation of the chemical structure of factor B. In conjunction with recombinant DNA studies by Dr. Ali Javed, this work promises important insights into the mechanism of proton conduction across the mitochondrial membrane.

One of the intriguing questions in membrane function is how the proteins embedded in the phospholipid bilayer interact with the phospholipid molecules. It is possible that the lipids, besides providing the insulating barrier, may also modulate the transport of molecules across the bilayer. Dr. Michael Pringle is studying this question by inserting the F_o proteins into different kinds of phospholipid bilayers to determine the effect on proton conductivity.

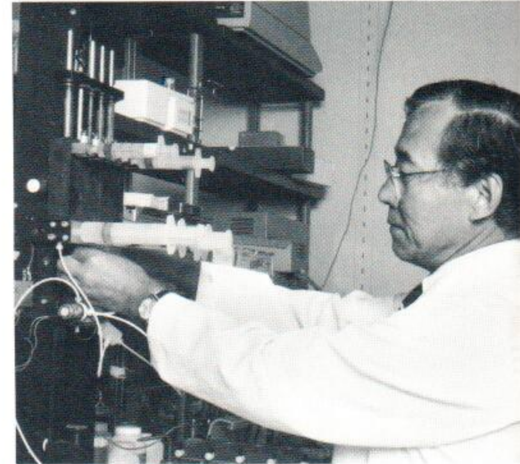


The actual arrangement of the proteins composing ATP synthase in a membrane bilayer.

POST AND TELEGRAPH

HOW DOES MUSCLE RESPOND TO NERVE SIGNALS?

The contraction of a muscle fiber is usually initiated by a nerve impulse, which triggers a local change of voltage across the muscle cell membrane. This voltage change travels along the so-called T-tubule, an extension of the cell membrane, to an intracellular calcium-storage granule, the sarcoplasmic reticulum (SR), to activate the release of calcium across the SR membrane. The increased calcium concentration in the cytoplasm acts on the muscle proteins to cause contraction. When contraction is completed, the calcium is pumped back into the SR. The mechanisms by which calcium leaves and reenters the SR are different: one is the downward flow from high concentration to low, the other is an uphill transfer from low to high concentration which requires energy input from ATP.



Dr. Noriaki Ikemoto measuring the rate of release of calcium across the SR membrane.

How the electrical signal is transmitted from the T-tubule to the SR membrane is a difficult and challenging problem. Dr. Noriaki Ikemoto and his group have made an important beginning by isolating from skeletal muscle a complex of T-tubule and SR which responds to changes in the ionic composition of the surrounding solution in the same manner as to an electrical signal. They are now using this preparation to study the mechanism that triggers calcium release.

Driving the calcium back into the SR involves a pump protein which has one site for calcium binding and transport across the membrane and another site for ATP binding and the use of its energy to drive the transport. Dr. Terry Scott has labeled these sites with luminescent analogs of calcium and ATP. When one of these, for example the calcium analog, is excited with light from a laser, it transfers some of the light energy to the other, for example the ATP analog. As a result of this energy transfer, the characteristics of the light that is emitted undergo a change, yielding a measure of the distance and the interaction between the two sites. This information, in conjunction with parallel studies on the structure of the calcium pump protein, is providing insights into the detailed molecular mechanism by which an ion pump can be energized by ATP.

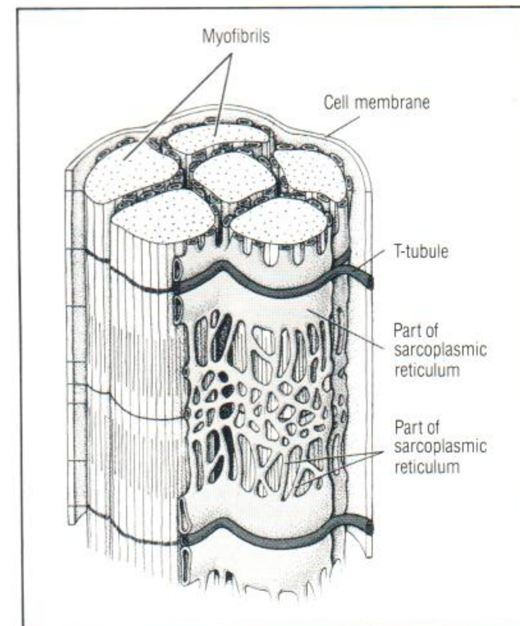


Diagram of muscle fibers with sarcoplasmic reticulum and T-tubules.

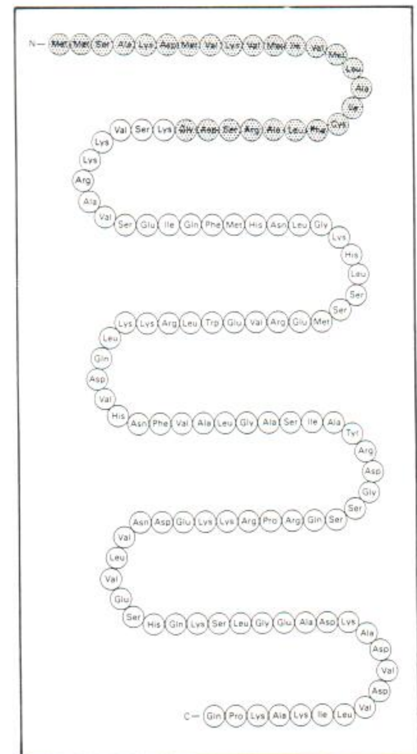
EXPORT CONTROLS

HOW ARE CERTAIN PROTEINS SECRETED ACROSS MEMBRANES?

Most proteins synthesized by the cell are for its own use and therefore always remain within the cell. This is as expected, for proteins generally have a hydrophilic surface and are thus unable to pass through hydrophobic membranes. Some cells, however, specialize in the export of certain proteins, such as hormones, antibodies, enzymes, and toxins. This raises two interesting questions: How can some proteins be designated for secretion and how can they cross the cell membrane? A partial answer to the first question is now known: Many proteins destined for secretion are first synthesized with a "signal" sequence which somehow informs a membrane component that they are allowed to leave the cell. On the other hand, the answer to the second question is still quite obscure because it has been difficult to separate the process of protein secretion from protein synthesis.

Drs. Phang Tai and Ling-Ling Chen discussing their experiments on protein secretion.

Dr. Phang Tai and his group are studying the secretion of enzymes and toxins by bacteria. By using membrane-free purified components required for protein synthesis and recombining them with purified membranes, they have been able to achieve protein synthesis and secretion across the membrane in separate steps and can thus study the characteristics of the secretion step. Dr. Tai made the important observation that protein secretion requires ATP as a source of energy. Using various inhibitors and mutants, Dr. Tai's group is now beginning to unravel the complex molecular mechanism of bacterial protein secretion.



Parathyroid hormone and its signal sequence (stippled). The signal sequence is needed only for hormone secretion but not for the hormone's function (bone formation).

ARMY AND NAVY

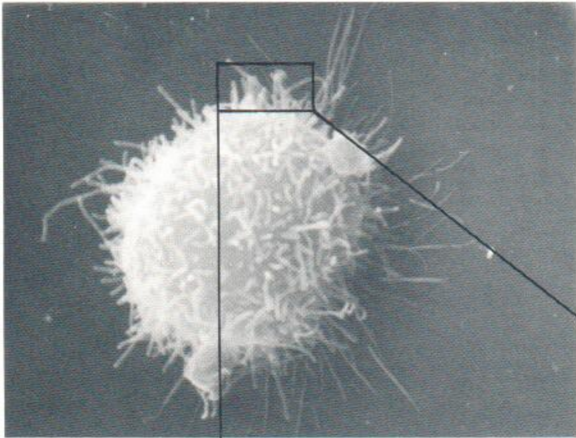
HOW DO CELLS PROTECT THEMSELVES AGAINST ATTACK?

An animal—including man—protects itself against foreign cells by attacking their membrane proteins with its immune system. This is the reason for the frequent rejection of transplanted tissues and also why tumors, recognized as "foreign" cells, are not more prevalent. Nevertheless, tumors do occur, and in many cases this is because they have somehow evaded the body's immune surveillance.

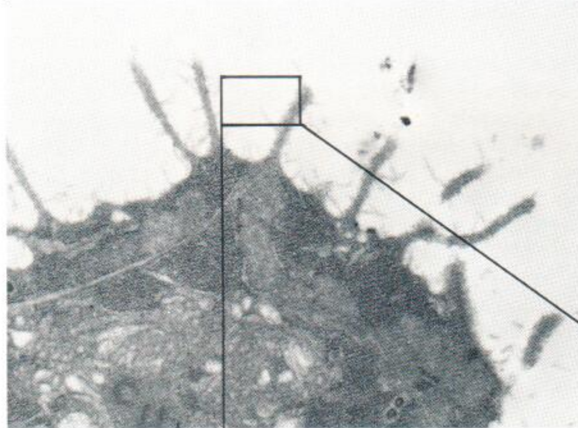
Dr. John Codington measuring the amount of epiglycanin in blood samples.

Dr. John Codington has found that certain types of carcinoma cells produce large amounts of an unusual membrane glycoprotein (a protein which is covered by many carbohydrate chains), which shields the more typical membrane proteins from immune attack. By studying the mechanism by which this glycoprotein, called *epiglycanin*, protects the cancer cells, Dr. Codington hopes to gain an understanding of one of the contributing factors to the spreading of cancer throughout the body and perhaps also an insight of how to counteract it. One possible clinical application of Dr. Codington's research seems particularly promising. Epiglycanin shows up in the blood of patients with carcinomas, and its early detection may provide a timely diagnosis for that form of cancer.

An individual's normal membrane proteins are tolerated by its immune system, but they will elicit the production of antibodies if they are injected into other animals. If such antibodies are linked to a toxin, they can be used to destroy cells that carry these particular proteins on their membranes. For example, a toxic chemical might be linked to an antibody that specifically binds to a protein which occurs on the surface of cancer cells but not on most normal cells. When injected into an animal, this drug will be specifically targeted to the cancer cells and destroy the tumor with little effect on normal tissue. Dr. Peter Davison is devising methods for linking potent toxins to specific antibody molecules, and Dr. Victor Raso, who is about to join BBRI as a faculty member, is exploring methods for the efficient delivery of such toxins across the cell membrane into the cytoplasm, where they can exert their lethal action.



A cell of a mouse tumor which has evaded attack by the immune system.



Magnified view of the tumor cell surface showing epiglycanin molecules branching from the surface protuberances.

Purified fibrous epiglycanin molecules isolated from the tumor cell.

THANK YOU!

The generosity of far-sighted foundations, individuals, and businesses this year provided a record $196,500 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.

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Center foreground: Dr. H. Gobind Khorana, Nobel Laureate; Theresa Raso. On the right, Newell Flather, Mary Jane Sanadi. At the left, Kate Flather; and Dr. Mohandas Kini, Corporation member.

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Mr. and Mrs. Robert Ingalls with Dr. Peter Davison, Deputy Executive Director, at left.

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Dr. Jen-Shiang Hong, Senior Scientist, explaining DNA sequencing at the Spring Open House.

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BOSTON BIOMEDICAL RESEARCH INSTITUTE
BALANCE SHEETS
AUGUST 31, 1987 AND 1986

	1987	1986
ASSETS		
CURRENT ASSETS		
Cash	$ 1,157,814	$ 1,079,087
Grants receivable	3,999,958	4,441,264
Pledges receivable		37,300
Prepayments, deposits and other receivables (note 7)	176,520	183,233
Investments, at market value (cost 1987—$2,871,030 1986—$2,355,204) (note 6)	3,373,969	2,928,113
Total current assets	8,708,261	8,668,997
FIXED ASSETS (notes 1 and 2)		
Leasehold improvements	1,935,632	1,935,632
Research equipment	3,971,086	3,567,053
Furniture and fixtures	48,799	48,799
Total	5,955,517	5,551,484
Less accumulated depreciation and amortization	3,934,164	3,644,678
	2,021,353	1,906,806
	$10,729,614	$10,575,803
LIABILITIES AND FUND BALANCES		
CURRENT LIABILITIES		
Accounts payable and accrued expenses	$ 80,855	$ 40,576
Overhead and fringe benefit adjustment payable	218,403	579,410
Deferred grant income (note 5)	4,417,742	4,762,971
Deferred fund (building) (note 5)	115,702	115,702
Total current liabilities	4,832,702	5,498,659
FUND BALANCES (note 1)		
Operating	1,003,961	747,075
Plant and equipment	2,364,028	1,977,234
Permanent research	507,570	446,029
Fixed assets (notes 1 and 2)	2,021,353	1,906,806
Total fund balances	5,896,912	5,077,144
	$10,729,614	$10,575,803

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, 1987 AND 1986

	1987	1986
REVENUES		
Grants	$5,702,938	$5,356,104
Equipment replacement	99,425	93,892
Contributions and bequests	222,599	175,775
Property and equipment purchased (notes 1 and 2)	404,033	238,754
Investment income	467,821	611,069
Total	6,896,816	6,475,594
EXPENSES (by department)		
Muscle Research	2,647,692	2,536,970
Cell Physiology	1,110,908	1,227,757
Fine Structure	544,010	521,623
Metabolic Regulation	1,146,687	881,385
General Research	247,370	199,085
Fund Raising	47,357	38,854
Purchase of fixed assets (note 1)	43,538	18,420
Depreciation and amortization (note 2)	289,486	234,267
Total	6,077,048	5,658,361
NET ADDITION TO FUNDS	819,768	817,233
FUND BALANCES, BEGINNING OF YEAR (note 1)	5,077,144	4,259,911
FUND BALANCES, END OF YEAR (note 1)	$5,896,912	$5,077,144

See accompanying notes to financial statements.

BOSTON BIOMEDICAL RESEARCH INSTITUTE
NOTES TO FINANCIAL STATEMENTS
AUGUST 31, 1987 AND 1986

(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 5).
- 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 $99,425 in 1987 and $93,892 in 1986. In addition, $43,538 of equipment was charged to the operating fund in the year ended August 31, 1987, $18,420 in 1986 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 research equipment and furniture 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) - DEFERRED COMPENSATION PLAN

The Institute has a deferred compensation plan, with funds held by an insurance company as custodian. The assets of the fund and the related deferred compensation liability are not included in the financial statements as they are not intended to be available for operations, but as a segregated retirement fund.

(5) - CHANGES IN DEFERRED RESTRICTED AMOUNTS

	1987			1986
	Building Fund	Grants & Contracts	Total	Total
Balance, beginning of year	$ 115,702	$ 4,762,971	$ 4,878,673	$ 4,765,953
Additions:				
New grants awarded		5,275,403	5,275,403	5,380,976
Contributions and pledges		6,495	6,495	1,541
Investment income	15,646	53,719	69,365	105,404
	131,348	10,098,588	10,229,936	10,253,874
Deductions:				
Funds expended for designated purposes		5,680,846	5,680,846	5,347,645
Transfer of investment income from Building fund	15,646		15,646	27,556
Balance, end of the year	$ 115,702	$ 4,417,742	$ 4,533,444	$ 4,878,673

(6) - 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.

(7) - BOSTON BIOTECHNOLOGY CORPORATION

The Institute has advanced $119,750 to Boston Biotechnology Corporation (see note 6). This amount is included in the category Prepayments, deposits and other receivables. At August 31, 1987, Boston Biotechnology Corporation was still in the development stage and had no significant liquid assets.

AUDITOR'S REPORT

Board of Trustees
Boston Biomedical Research Institute
Boston, Massachusetts

I have examined the balance sheets of Boston Biomedical Research Institute as of August 31, 1987 and 1986, 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, 1987 and 1986, 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
(617) 449-5545

September 24, 1987

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Photography
Cover photo: John Ganson, photographer. —Dr. Peter Davison, Deputy Executive Director and Director of the Department of Fine Structure Research, examining bacterial membranes under the electron microscope.

Tad Goodale: Photos on pages 5,6,8,9,10,11,12; 2nd and 3rd on page 15; 16,17

Fay Foto: page 14; 1st on page 15.

John Ganson: pages 2,3,7.

Scott C. Miller, Ph.D.: page 13, top and middle photos.

Henry S. Slater, Ph.D.: page 13, bottom photo.

Quote
Inside front cover: Doris Brody, from the brochure "Then & Now—Biomedical Science in 1887 & Today."

We thank John Ganson, photographer, for the generous donation of his time and talent.

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Quote
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