THE AMERICAN PHYSIOLOGICAL SOCIETY

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The Physiologist

A Publication for Physiologists and Physiology
Orr E. Reynolds, Editor

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Please Note: Society Business and Notices are on gray-edged paper.

CURRENT SCHEDULE OF FUTURE MEETINGS

1977 – International Physiological Congress – Paris, France – July 18-23
1977 Fall – Hollywood Beach, Florida – October 9-14
1978 Spring – Atlantic City, New Jersey – April 9-14
1978 Fall – St. Louis, Missouri – October 22-27
1978 Fall – Campus Specialty Meeting – Michigan State – Categorical Subject and Date to be announced
1979 Spring – Dallas, Texas – April 8-13
1979 Fall – New Orleans, Louisiana – October 14-19
1980 Spring – Anaheim, California – April 13-18
1980 Fall – Miami Beach, Florida – October 12-17
1981 Spring – Atlanta, Georgia – April 12-17
1981 Fall – Boston, Massachusetts – November 1-6
1982 Spring – New Orleans, Louisiana – April 18-23
1982 Fall – San Diego, California – October 10-15

PHILIP BARD 1898 - 1977

Philip Bard died in California on April 5, 1977. He was at that time Professor of Physiology, Emeritus, and Director of the Department, Emeritus, of the Johns Hopkins University, posts which he had filled from 1933 to 1964; he had served as dean of the Medical Faculty at Hopkins for four years, 1953-1957.

Bard was born in Hueneme (now Port Hueneme), California in 1898, the son of Thomas Robert Bard and Mary Beatrice (Geberding) Bard. His father was a distinguished citizen of California who played an important role in the cultural and economic development of his state; he served it as United States Senator, 1901-1905. Philip Bard was educated first in a primary school in Pasadena, California, and in 1913 entered the Thacher School in the Ojai Valley of Ventura County, California. His experience in this school had a lasting influence on his life; he served later as a member of its Board of Trustees (1965-1977), and at the end of his life returned to live near it. It is of interest that by the age of 16, after only two years in the Thacher School, he had developed an interest in Biomedical Research which persisted all his life, had obtained and read through the 1905 edition of Howell's Textbook of Physiology, and had made his first attempt at physiological experimentation, in the attic of his home! Dr. Bard himself always denied having shown any signs of academic excellence during his time in school, describing instead his devotion to baseball and horsemanship, and indeed he failed four of the six entrance examinations for Princeton University early in 1917. (He was to graduate from that University in its class of 1923 with highest honors in Biology.)

In June of 1917 Bard volunteered to the Stanford unit of the U. S. Army Ambulance Corps, and served through six campaigns of World War I in France. In 1919, upon his return to California, he sought advice about his future career from the great San Francisco internist, Walther Alvarez, his family physician. The latter encouraged Bard's interest in biomedical research, told him of his own experience in Walter Cannon's laboratory at Harvard, and guided him to Bayliss' Principles of General Physiology. Thus upon entering Princeton (with conditions!) in the fall of 1919, Bard had already studied two of the great classics on Physiology then extant in the English language, Howell and Bayliss. While a junior at Princeton he married Harriet Hunt of Pasadena, California. Their marriage was a long and happy one, blessed with two daughters, who survive.

At Princeton, Bard quickly absolved his entrance conditions; in some way he was allowed to substitute an extensive knowledge of Latin for a glaring deficiency in Mathematics! He came under the influence of two of the most productive and distinguished Biologists of the day, Edwin Grant Conklin and E. Newton Harvey. It was the latter who reinforced his student's appreciation of the beauty and joy to be found in biological research, and influenced Bard's decision to abandon Medicine as a career – he had in his senior year at Princeton been admitted to the Johns Hopkins University School of Medicine. Bard spent a fifth year at Princeton better to prepare himself for his research career, and in the fall of 1924 entered the Division of Medical Sciences at Harvard University, to work for the Ph.D. degree under the direction of Professor Walter Cannon.

One can appreciate the intellectual excitement of the Cannon laboratory in the 1920's, and its effect upon an entering graduate student. The senior staff was composed of individuals with international reputations, and great accomplishment: Cannon, Forbes, Redfield, Drinker, Davis, and Castle. The central theme of Dr. Cannon's own investigations was the autonomic nervous system, and almost every aspect of the system was under study. It was the central nervous mechanisms in emotional expression which attracted Bard's continuing interest, and became the subject of his thesis research and of many studies which followed it. In the former he showed that the integration of sympathetic and somatic efferent discharge that characterizes the expression of rage depends upon the integrity of the posterior hypothalamus; only fragments of that fully patterned reaction appear with lower truncations of the brain stem. The excessive and readily evoked "quasi-emotional" behavior displayed by decorticated carnivores was conceived to be an example of the release of function, in the tradition of the ideas of Jackson and of Head. Perhaps more importantly, this first study provided an objective definition of a neural center, a concept that guided the later research of many investigators. It also influenced in a profound way the developing field of Physiological Psychology. The integrating and regulating function of the hypothalamus was then pursued by Bard in a long series of studies with a number of colleagues, at Princeton (1928-1931), once again at Harvard (1931-1933) and from 1933 on at Johns Hopkins. They include, in addition to the central neural mechanisms for the expression of rage and fear, studies of the hypothalamic function in regulating sexual behavior and the reproductive cycle, in governing the pituitary gland and its target organs, in the regulation of body temperature, and in the production of fever.

In March of 1933 (he was then 34 years old) Bard received a formal invitation by letter from the president of the Johns Hopkins University to join its faculty as Professor of Physiology, and Director of the Department of Physiology in its School of Medicine. Although he had in

the previous year paid a social visit to Baltimore, he had previously no inkling of this offer, no invitation for hour-long interviews with members of the search committee, no preliminary negotiations whatsoever. He had published only four papers and two reviews, and considered himself a beginner. The appointment was wholly in the tradition of the institution he joined; quietly to seek out the most promising young man in a field, give him free rein to develop it, and take whatever chances for error attending such audacious behavior. Seldom in its history has such a typical Hopkins appointment met with such widespread approval, and long-term success. Thus Bard succeeded to the chair held originally by William H. Howell, the man whose writings had first aroused his desire to do physiological research, nearly 20 years earlier. Bard was to hold that chair for a period of 31 years.

Dr. Bard related that upon his arrival in Baltimore he found himself in a peculiar and unexpected, and in some ways an embarrassing position. He was at once accepted by his distinguished senior colleagues as a scholar with impeccable credentials, quite equal to their own. He found a Dean and an administration that considered its sole function to be to serve the needs of the faculty. He was given complete authority in all matters relating to Physiology — staff, research and teaching program, etc.; along with it went total responsibility. Though his resources were small, he rejuvenated a small department, induced Chandler Brooks and Clinton Woolsey to join him in associations that lasted for many years, and initiated with them a program of research in the Physiology of the Nervous System.

Dr. Bard had taken up, before leaving Harvard, the general problem of the localization of function in the cerebral cortex, particularly in the motor and sensory cortices, his measure was the integrity of the placing and hopping reactions. Bard carried out, with Woolsey and Brooks, an extensive comparative study of the cortical control of these reactions, showed their increasing degree of corticalization in phylogeny, their loss following discreet local lesions of the somatotopically related portions of the sensory and motor cortices, and by their integrity the remaining capacity for function of similarly located small surviving remnants. These studies perhaps represent the limit to which the method of surgical ablation and clinical examination can be pushed in elucidation of cortical function. They culminated in Bard's Harvey lecture of 1938.

Shortly before that time Wade H. Marshall had introduced the evoked potential method into the Hopkins Laboratory. Dr. Bard participated in the earliest of the mapping studies of the postcentral gyrus in the monkey, with Woolsey and Marshall. Thereafter he left this method to flower in the hands of Woolsey and the latter's colleagues and students, and returned to his earlier interests in the central neural mechanisms controlling emotional behavior, and the regulatory functions of the hypothalamus.

The education paradigm Bard found at Hopkins differed somewhat from that he had known at Harvard and at Princeton. The first responsibility was then, as it has continued to be, the education and maturation of students of Medicine; the second was the further polishing of young faculty members for posts elsewhere; the third was the training in research of postdoctoral fellows. Dr. Bard excelled in all of these, and particularly in the education of medical students. His influence upon them was direct and profound, he had scarcely a peer in the teaching of basic medical science. He taught in a very personal way, gave a course with the minimal number of lectures, and emphasized individual initiative, free time for scholarly endeavor, and the small group laboratory exercise. The latter was used by him to bring teacher and taught into direct dialogue around a naturally occurring problem, to enhance the student's powers of observation and reasoning, and to teach him to evaluate evidence critically. In this his ideas resembled those of Franklin Pain Mall, whom he greatly admired, and Bard was continually distressed by what he considered the disastrous move to eliminate or greatly reduce laboratory experience in many courses of Physiology in recent years. Of the 31 classes of Hopkins students who passed through his department during his tenure, scarcely a graduate exists but recalls him with respect and affection. For many it was he who taught them something unforgettable, the artistic beauty to be found and revealed in the scientific enquiry into the physiological basis of Medicine.

In his department Bard created an atmosphere of the ideal academic life. He led each of his intimate associates to understand that he had the Professor's complete confidence, that we were all embarked on a noble enterprise whose importance transcended all trivia, and that each of us was free to pursue his own interests and ideas, no matter where they led. Bard always seemed able to discover and turn to the light the best qualities of those about him, and to let them grow and develop to the full in their own personal ways. With that freedom went what he had himself received, total responsibility.

He received in his lifetime many honors — degrees, memberships in distinguished academies, presidencies of national societies, etc. He bore them modestly, not really believing he deserved them. He treasured most, I believe, his trusteeships of the Rockefeller University and of the Thacher School, and his membership in the American Philosophical Society, whose meetings he seldom missed. He served as President of the American Physiological Society during the years of the second World War, and thereafter contributed greatly to putting our publication enterprise on a firm financial basis.

Harriet Hunt Bard died in 1963. Thereafter, Dr. Bard married an old friend and sister of a former colleague, Janet MacKenzie Rioch, and together they enjoyed ten years of Bard's retirement. During that time he continued productive laboratory investigations, but insisted on working alone, with no students, no fellows, no grant, and no secretary: he pursued his own interests for the simple joy of it! He travelled widely, and gave much time to his trustee responsibilities, including that as President of the International Foundation. Janet Rioch Bard died in 1974; thereafter, Dr. Bard married Colleen Gillis, who survives him.

He was in his person tall and powerfully built, his features regularly formed in heavy granite, his eye a piercing, pale blue. He possessed great charity for the opinions of others, and avoided disputation; in counsel he was wise, modest, and persuasive. He radiated an ambient spirit of good humor, friendliness, and a fond concern for those about him.

That is how we shall remember him.

Vernon B. Mountcastle

MEMBERSHIP STATUS

	April 1, 1977
Regular Members	4,026
Retired Members	362
Honorary	13
Associate	576
Retired Associate	3
Corresponding	3
	4,983

SUSTAINING ASSOCIATES

Abbott Laboratories
Burroughs Wellcome Co.
CIBA Geigy Corp.
Grass Instrument Co.
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Hoffman-LaRoche, Inc.
Eli Lilly Co.
Merck Sharp & Dohme Res. Labs.
Norwich Pharmacal Co.
Pfizer, Inc.
A. H. Robins Co., Inc.
Smith, Kline and French Labs.
Warner-Lambert Research Inst.
Williams & Wilkins Co.
Wyeth Laboratories, Inc.

DEATHS REPORTED SINCE THE 1977 FALL MEETING

Carl S. Alexander — VA Hospital, Minneapolis
William R. Amberson (R) — 12-76
Robert M. Bird — 12-31-76 — National Library of Medicine, Bethesda, Md.
Robert V. Brown (R) — 7-1-76
Savino A. D'Angelo — 8-18-76 — Thomas Jefferson Univ., Philadelphia
Leo Di Cara — 8-23-76 — Univ. of Michigan Mental Health Res. Inst., Ann Arbor
Smith Freeman — Consultant, G. S. Searle & Co., Skokie, Ill.
James Kollias — 3-10-77 — Pennsylvania State Univ., University Park
Ross A. McFarland (R) — 11-7-76 — Harvard School of Public Health, Boston
David Marine (R) — 11-26-76
Clifford T. Morgan — 2-11-76 — University of Texas, Austin
Nasser S. Nejad — Illinois Inst. of Technology, Chicago
James Olds — 8-21-76 — California Inst. of Technology, Pasadena
Jean R. Oliver (R) — 11-19-76
Robert A. Phillips — 9-17-76
Charles A. Ragan, Jr. (R) — 10-26-76 — Columbia Univ., Coll. of P & S, New York
Robert I. Weed — 8-18-76 — Univ. of Rochester Sch. Med., Rochester, NY
Charles W. Urschel — 2-27-77 — Univ. of South Alabama Coll. Med., Mobile

50 YEAR MEMBERS

Adolph, Edward F.
Alvarez, Walter C.
Bergeim, Olaf
Best, Charles H.
Blumbart, Herrmann L.
Cattell, McKeen
Davis, Hallowell
Gilson, Arthur S.
Greisheimer, Esther M.
Gross, Erwin G.
Hastings, Albert B.
Hertzman, Alrick B.
Higgins, Harold L.
Hitchcock, Fred A.
Irving, Laurence
Ivy, Andrew C.
Jackson, Dennis E.
Kleitman, Nathaniel
Koppanyi, Theodore
Leake, Chauncey D.
Lee, Milton O.
McClendon, Jesse F.
McCouch, Grayson P.
Miles, Walter R.
Miller, Frederick R.
Minot, Ann S.
Pond, Samuel E.
Rapport, David
Redfield, Alfred C.
Reznikoff, Paul
Richter, Curt P.
Ryan, Andrew H.
Van Liere, Edward J.
Visscher, Maurice B.
Wearn, Joseph T.
White, Harvey L.
Wulzen, Rosalind
Wyman, Leland C.

NEWLY ELECTED MEMBERS

The following, nominated by Council, were elcted to membership in the Society at the Spring Meeting, 1977.

AIELLO, Edward L.: Dept. Biol. Sci., Fordham Univ., Bronx, N.Y.
ARRUDA, Jose A. L.: Sect. Nephrology, Univ. of Illinois Hosp., Chicago
BAGSHAW, Roger J.: Asst. Prof., Haverford, PA
BALDWIN, Kenneth M.: Dept. Physiol., Univ. of California, Irvine
BANTLI, Heinrich: Dept. Neurosurg., Univ. of Minnesota, Minneapolis
BELLINGER, Larry L.: Dept. Physiol., Baylor Coll. Dent., Dallas
BENNETT, Albert F.: Dept. Cell Biol., Univ. of California, Irvine
BERGER, Albert J.: Dept. Physiol., Univ. of Californa, San Francisco
BERKLEY, Karen J.: Dept. Psychol., Florida State Univ., Tallahassee
BHALLA, Ramesh C.: Dept. Anat., Univ. of Iowa, Iowa City
BIANCANI, Piero: Dept. Int. Med., Yale Univ., New Haven, CT
BISHOP, Charles W.: Buffalo General Hospital, Buffalo, N.Y.
BLOOM, Sherman: Dept. Pathol., Univ. of South Florida, Tampa
BOHLEN, Harold G.: Dept. Physiol., Indiana Univ. Sch. Med., Bloomington
BOOTH, Frank W.: Dept. Physiol., Univ. of Texas Med. Sch., Houston
BREAZILE, James E.: Dept. Vet. Anat.-Physiol., Univ. of Missouri, Columbia
BROOKES, Victor J.: Dept. Entomol., Oregon State Univ., Corvallis
BROWN, Marvin R.: Salk Inst., Lab. Neuroendocrinol., San Diego
BUCKALEW, Vardaman, M., Jr.: Dept. Med., Bowman Gray Sch. Med., Winston-Salem
CARLSON, Edwin L.: Res. Assoc., Stanford Univ., Stanford, CA
CASABURI, Richard: Div. Resp. Physiol. & Med., Harbor Gen. Hosp., Torrance, CA
CEREIJIDO, Marcelino: Dept. Fisiol., Centro de Invest., Mexico
CHAN, Po Chuen: Naylor Dana Inst., Am. Health Fndn., Valhalla, N.Y.

CHEN, Chao-ling D.: Coll. Vet. Med., Univ. of Florida, Gainesville

CHENG, Thomas C.: Inst. Pathobiol., Lehigh Univ., Bethlehem, PA

CLARK, Mary E.: Biol. Dept., San Diego State Univ., San Diego

CLARK, Nancy B.: Biol. Sci. Group, Univ. of Connecticut, Storrs

COULSON, Richard L.: Sect. of Cardiol., Temple Univ. Hlth. Sci. Ctr., Philadelphia

COULTER, Dwight B.: Dept. Physiol. & Pharmacol., Univ. of Georgia, Athens

CROWE, John H.: Dept. Zool., Univ. of California, Davis

DAVIS, Walter L.: Dept. Microanat., Baylor Coll. Dentistry, Dallas

De SIMONE, John A.: Dept. Physiol., Medical College of Virginia, Richmond

DEVROEDE, Ghislain: Dept. Surg., Ctr. Hosp. Univ., Quebec

DIETER, Michael P.: Patuxent Wildlife Res. Ctr., Laurel, MD

DIETZ, Thomas H.: Dept. Zool. & Physiol., Louisiana State Univ., Baton Rouge

DRAZEN, Jeffrey M.: Dept. Med., Peter Bent Brigham Hosp., Boston

DUNN, Michael J.: Dept. Med., Univ. of Vermont, Burlington

DUPONT, Andre: Lab. Molecular Endocrinol., CHUL, boul. Laurier, Quebec

EDGERTON, V. Reggie: Dept. Kinesiology, UCLA, Los Angeles

EDMUNDS, L. Henry, Jr.: Univ. of Pennsylvania, Philadelphia

ESKIN, Arnold: Biol. Dept., Rice Univ., Houston

EVANS, David H.: Dept. Biol., Univ. of Miami, Coral Gables

FEIGEN, Larry P.: Dept. Physiol., Tulane Med. Ctr., New Orleans

FIORINDO, Robert P.: Dept. Physiol., Ohio State Univ., Columbus

FLEMING, Donovan E.: Dept. Psychology, Brigham Young Univ., Provo, Utah

GANJAM, Venkataseshu K.: Sch. Vet. Med., Univ. of Pennsylvania, Philadelphia

GARDNER, Esther P.: Dept. Physiol., NYU Sch. Med., New York, N.Y.

GARNER, Duane L.: Dept. Physiol. Sci., Oklahoma State Univ., Stillwater

GOTSHALL, Robert W.: Dept. Physiol., Wright State Univ., Dayton, Ohio

GRUBB, Robert L., Jr.: Dept. Neurosurg., Washington Univ., St. Louis

HADLEY, Neil F.: Zool. Dept., Arizona State Univ., Tempe

HAGEMAN, Gilbert R.: Dept. Physiol. & Biophys., Univ. Alabama, Birmingham

HARKEN, Alden H.: Div. Cardiothoracic Surg., Hosp. of Univ. of Pennsylvania

HARRIS, Robert H., Jr.: Div. Nephrol., Duke Univ. Med. Ctr., Durham, NC

HAYMOVITS, Asher: Downstate Med. Ctr., Brooklyn, NY

HENRY, James L.: Anesthesia Res. Dept., McGill Univ., Montreal

HILL, Esther P.: Dept. Med., Univ. of California, S.D., La Jolla

HISAW, Frederick L., Jr.: Dept. Zool., Oregon State Univ., Corvallis

HUNT, Jack N.: Dept. Physiol., Baylor Coll. Med., Houston

KACHADORIAN, William A.: Renal Service, USPHS Hosp., Staten Island, NY

KALRA, Satya P.: Dept. Ob/Gyn., J. Hillis Miller Hlth. Ctr., Gainesville, FL

KAO, Race Li-Chan: Dept. Physiol., Pennsylvania State Univ., Hershey

KARDON, Merrill B.: Physiologist, Metairie, LA

KATZENELLENBOGEN, Benita S.: Dept. Physiol., Univ. of Illinois, Urbana

KELSEN, Steven G.: Hosp. of Univ. of Pennsylvania, Philadelphia

KILGORE, Delbert L., Jr.: Dept. Zool., Univ. of Montana, Missoula

KLICKA, John K.: Biol. Dept., Univ. of Wisconsin, Oshkosh

KNAUF, Philip A.: Res. Inst., Hosp. for Sick Children, Toronto

KOERKER, Donna J.: Div. Endocrinol., Harborview Med. Ctr., Seattle

KOW, Lee-Ming: Rockefeller Univ., New York, NY

KUNZE, Diana L.: Dept. Physiol. & Biophys., Univ. of Texas Med. Br., Galveston

LANG, Michael A.: Dept. Physiol., Boston Univ. Sch. Med., Boston

LEE, Chin Ok: Dept. Physiol. & Biophys., Cornell Univ. Med. Coll., New York

LEVITZKY, Michael G.: Dept. Physiol., Louisiana State Univ. Med. Ctr., New Orleans

LI, Jeanne B.: Dept. Physiol., Hershey Med. Ctr., Hershey, PA

LIPTON, Peter: Dept. of Physiol., Univ. of Wisconsin, Madison

McMURTRY, Ivan F.: CVP Res. Lab., Univ. of Colorado Med. Ctr., Denver

MAXWELL, Leo C.: Dept. Physiol., Univ. of Michigan Med. Sch., Ann Arbor

MESSINA, Edward J.: Dept. Physiol., New York Med. Coll., Valhalla

MILLER, David S.: Mount Desert Island Biol. Lab., Salsbury Cove, ME

MOON, Thomas W.: Dept. Biol., Univ. of Ottawa, Ottawa, Ont., Canada

MORISHIGE, Walter K.: Dept. Physiol., Univ. of Hawaii Sch. Med., Honolulu

MORTILLARO, Nicholas A.: Dept. Physiol., Univ. of South Alabama, Mobile

NATTIE, Eugene E.: Dept. of Physiol., Dartmouth Med. Sch., Hanover, NH

NIGHTINGALE, Thomas E.: USDA Poultry Res. Lab., Georgetown, DE

NORRIS, Jeanne E.: George Williams College, Downers Grove, IL

OJEDA, Sergio R.: Dept. Physiol., Univ. of Texas Hlth. Sci. Ctr., Dallas

PARSONS, Robert H.: Dept. Biol., Rensselaer Polytech. Inst., Troy, NY

PASSMORE, John C.: Dept. Physiol. & Biophys., Univ. of Louisville Hlth. Sci. Ctr.
PETROFSKY, Jerrold S.: Dept. of Physiol., St. Louis Univ., St. Louis, MO
PHILLIPS, John E.: Dept. Zool., Univ. British Columbia, Vancouver
POISNER, Alan M.: Dept. Pharmacol., Univ. of Kansas Med. Ctr., Kansas City, KS
PRITCHARD, Austin W.: Zool. Dept., Oregon State Univ., Corvallis
QUADRI, S. Kaleem: Oregon Primate Res. Ctr., Beaverton
RAO, Ch. Venkateswara: Dept. OB-GYN, Univ. of Louisville
RAY, Tushar K.: Dept. Physiol., Univ. of Texas Hlth. Sci. Ctr., Houston
REDDI, A. Haridara: Ben May Lab. for Cancer, Univ. of Chicago
REUSS, Luis: Dept. Physiol. & Biophys., Washington Univ. Med. Sch., St. Louis
RODBARD, David: Natl. Insts. of Health, Bethesda, MD
RUSSELL, Raymond A.: Dept. Physiol., Louisiana State Univ., New Orleans
SAARI, Jack T.: Dept. Basic Sci., Marquette Univ., Milwaukee
SANDERS, Tommy M.: Pathol. Dept., Univ. of California, S.D., La Jolla
SHRIVASTAV, Brij B.: Dept. Physiol. & Pharmacol., Duke Univ. Med. Ctr., Durham
SLONIM, Arnold R.: Res. Chem., Aerospace Med. Res. Lab., Dayton, OH
SMITH, Dean O.: Dept. Physiol., Univ. of Wisconsin Med. Sch., Madison
SMITH, Delmont C.: Dept. Biol. Sci., State Univ. Coll., Brockport, NY
SOKOLOVE, Phillip G.: Dept. Biol. Sci., Univ. of Maryland, Catonsville, MD
SOMERO, George N.: Scripps Inst. of Oceanography, La Jolla, CA
STAHL, Philip D.: Washington Univ. Sch. Med., St. Louis, MO
STEGER, Richard W.: Wayne State Univ. Sch. Med., Detroit
STETSON, Milton H.: Sch. Life & Health Sci., Univ. of Delaware, Neward
THORNBURG, Kent L.: Dept. Physiol., Univ. Oregon Hlth. Sci. Ctr., Portland
TOWLE, David W.: Dept. Biol., Univ. of Richmond, Richmond, VA
TSAGARIS, Theofilos J.: Cardiol. Sect., VA Hosp., Salt Lake City
ULRYCH, Milos: Dept. Med., Univ. of Mississippi Med. Ctr., Jackson
UMMINGER, Bruce L.: Dept. Biol. Sci., Univ. of Cincinnati, Cincinnati, OH
VOOGT, James L.: Dept. Physiol. & Biophys., Univ. of Louisville Sch. Med.
VOROSMARTI, James, Jr.: Naval Med. Res. Inst., Bethesda, MD
VREIM, Carol E.: Div. of Lung Dis., Natl. Insts. Health, Bethesda, MD
WADE, James B.: Dept. Physiol., Yale Univ. Sch. Med., New Haven, CT
WALD, Alvin S.: New York Univ. Med. Ctr., New York, NY
WALSH, John H.: Dept. Med., UCLA Sch. Med., Los Angeles
WEKSLER, Babette B.: Dept. Med., Cornell Univ. Med. Coll., New York, NY
WIKMAN-COFFELT, Joan: Dept. Med., Univ. of California, Davis
WILSON, Michael J.: Toxicol. Res. Lab., VA Hosp., Minneapolis
WITTY, Robert T.: Dept. Med., Wright State Univ. Sch. Med., Dayton, OH
YELLIN, Edward L.: Albert Einstein Coll. Med., Bronx, NY
YOUNG, Leona G.: Dept. of Physiol., Emory Univ., Atlanta, GA
ZUPERKU, Edward J.: Research Service, VA Hosp., Wood, WI

CORRESPONDING MEMBERS

DEJOURS, Pierre: Lab. Resp. Physiol., Ctr. Natl. Recherche, Strasbourg, France
VANHOUTTE, Paul M.: Dept. Int. Med., Univ. Instelling Antwerp, Belgium

ASSOCIATE MEMBERS

ABZUG, Charles: Dept. Physiol., Univ. of Maryland, Baltimore
ACKERMAN, Ralph A.: Dept. Physiol., State Univ. of N.Y., Buffalo
BAGBY, Gregory J.: Dept. Physiol., Louisiana State Univ., New Orleans
BARBER, Billy J.: Dept. Physiol., Bowman Gray Sch. Med., Winston-Salem, NC
BEYENBACH, Klaus W.: Dept. Physiol., Univ. of Arizona, Tucson
BLACKWELL, Richard E.: Dept. OB/GYN, Univ. of Alabama, Birmingham
*BROOKS, Virginia L.: Dept. Physiol., Univ. of Michigan, Ann Arbor
BROWN, Harvey V.: Resp. Med., Harbor Gen. Hosp., UCLA Sch. Med.
CHAMBERS, Janice: Res. Assoc., Mississippi State Univ., Mississippi State, MS
DAWSON, Margaret A.: Natl. Marine Fisheries Service, Milford, CT
DeROTH, Laszlo: Biomed. Sciences, Univ. of Guelph, Guelph, Ont., Canada
EULER, David E.: Dept. Physiol., Loyola Univ. Med. Ctr., Maywood, IL
FERGUSON, James L.: Dept. Physiol., Louisiana Univ. Med. Ctr., New Orleans
*FISHER, Stephen J.: Dept. Physiol., Univ. of Michigan Med. Sch., Ann Arbor
FRANCIS, Kennon T.: Dept. Phys. Therap., Univ. of Alabama, Birmingham
GEIS, G. Steven: Dept. Physiol., Loyola Univ. of Chicago, Maywood, IL
HARDER, David R.: Dept. Physiol., Med. Coll. of Wisconsin, Milwaukee

JOHNSON, Larry R.: Dept. Physiol., Univ. of Oregon Hlth. Sci. Ctr., Portland

JOHNSON, Michael D.: Dept. Physiol., Harvard Med. Sch., Boston

KANEKO, Kenzo: Cardio-Resp. Lab., Orthopaedic Hosp., Los Angeles

KINNAMON, Kenneth E.: Dept. Physiol., Uniformed Services Univ. Hlth. Sci., Bethesda, MD

KIRK, Gerald R.: Oklahoma Coll. Osteopathic Med. & Surg., Tulsa

KOEHLER, Raymond C.: Dept. Physiol., State Univ. of N.Y., Buffalo

LORENZEN, Janice R.: Dept. Biol. Sci., Northwestern Univ., Evanston, IL

MICHELS, David B.: Dept. Med., Univ. California, S.D., La Jolla

MURRAY, Robert D.: Dept. Physiol., Univ. of Michigan, Ann Arbor

NELSON, Thomas E.: Dept. Anesthesiol., Univ. of Texas Med. Br., Galveston

OHATA, Carl A.: Marine Biomed. Inst., Univ. of Texas Med. Br., Galveston

*PEARCE, William J.: Dept. Physiol., Univ. of Michigan, Ann Arbor

PEAVY, Daniel E.: Dept. Physiol., Milton S. Hershey Med. Ctr., Hershey, PA

PHAIR, Robert D.: Dept. Physiol., Univ. of Michigan, Ann Arbor

RIDDLE, Wayne A.: Dept. Biol., Univ. of New Mexico, Albuquerque

ROBERTSON, Howard T. II: Dept. Med., Univ. Hospital., Seattle

ROKITKA, Mary A.: Dept. Physiol., State Univ. of N.Y., Buffalo

*ROMANOSKY, Albert J.: Pennsylvania State Univ., University Park, PA

ROSS, Brian K.: Dept. Med., Univ. of Washington, Seattle

SCHNEEMAN, Barbara O.: Nutrition Dept., Univ. of California, Davis

STREMEL, Richard W.: Div. Resp. Physiol., Harbor Gen. Hosp., Torrance, CA

TERRIS, James M.: Dept. Physiol., Univ. Michigan, Ann Arbor

THOMAS, John X., Jr.: Dept. Physiol., Loyola Stritch Sch. Med., Maywood, IL

URBSCHEIT, Nancy L.: Physical Therapy, Univ. of Iowa, Iowa City, IA

VENTERS, Michael D.: Dept. Physiol., Lovelace-Bataan Med. Ctr., Albuquerque

WEBB, R. Clinton: Dept. Physiol., Univ. of Michigan, Ann Arbor

WEISER, Philip C.: Dept. Clin. Physiol., Natl. Asthma Ctr., Denver

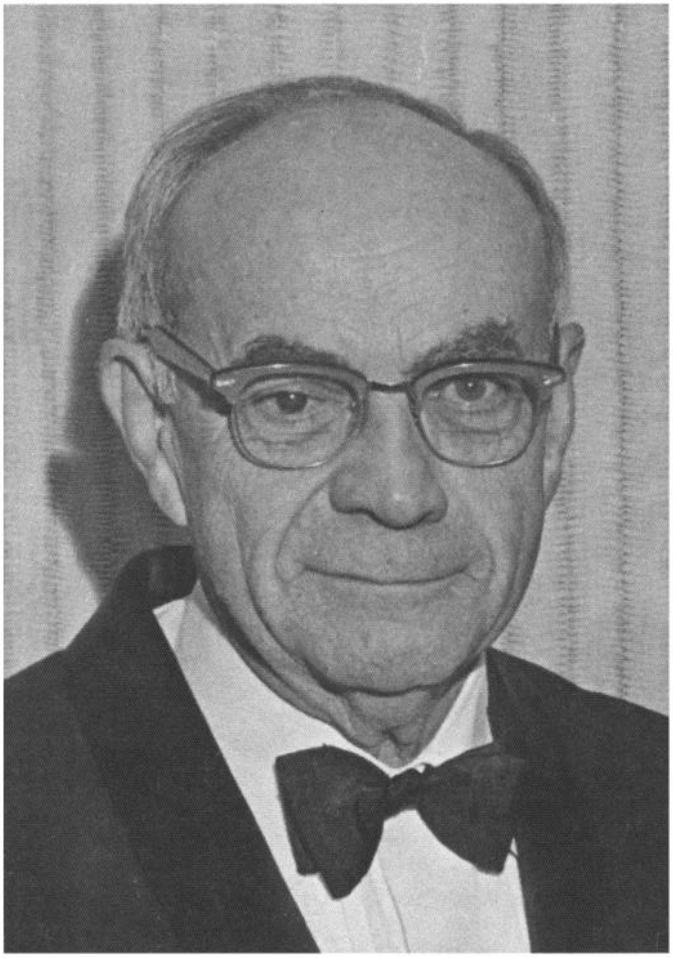
WILLIAMS, Carole A.: Dept. Physiol., St. Louis Univ., St. Louis, MO

WILSON, J. Roger: Dept. Psychiatry, Univ. of Michigan, Ann Arbor

WRIGHT, Kenneth C.: Vet. Physiol. & Pharmacol., Texas A & M, College Station

*Elected to Associate Membership but subsequently selected the new Student Membership.

RAY G. DAGGS AWARD



The 4th Daggs Award was presented to Dr. Julius Comroe by Dr. Selkurt at the Spring Meeting in Chicago. The Award is given in honor of the Society's past Executive Secretary, Dr. Ray G. Daggs. Dr. Selkurt presented the Award with these words.

"It is with great pleasure that I announce that the recipient of the 1977 Daggs Award is Dr. Julius H. Comroe, Morris Herzstein Professor of Biology at the University of California, San Francisco, and the first director of UCSF's Cardiovascular Institute in the period 1957 to 1973. In essence this Award is made by the Selections Committee based on past service to the American Physiological Society and to our science in general. Needless to say, the caliber and renown of today's recipient permeates more widely into medicine and biology than this. His fame is broadly based on his administrative leadership, ability as an investigator in cardiopulmonary physiology, his skill as a teacher, on his numerous publications, both scientific papers and texts, and last but not least, on his interest in the interrelationship of government to science and research support. His concern here has been the national debate on basic biomedical research vs. so-called 'targeted research.' His latest activity has involved 'researching the very act of research itself.'

"Dr. Comroe was born in York, Pennsylvania, the second son of a physician father and school teacher mother. He received his undergraduate training and his

medical degree with high honors from the University of Pennsylvania in 1934. He served an internship at the University of Pennsylvania Hospital (1934-36) and a research fellowship under Sir Henry Dale (1938). In 1936, Dr. Comroe began teaching at his alma mater. He was Professor and Chairman of the Department of Physiology and Pharmacology at the University of Pennsylvania Graduate School of Medicine from 1946 to 1957 when he came to UCSF as Professor of Physiology and the first Director of the newly established Cardiovascular Institute.

"Dr. Comroe became a member of the American Physiological Society in 1943. He served on the APS Council from November 1947 through May 1960. He was made President of the Society for the year 1960-61. He served on the Editorial Board of AJP from 1947 to 1951 and continued on the combined AJP/JAP format Editorial Board from 1952 to 1953. He was editor of Physiology for Physicians, the first edition published in 1963, and served as editor of Physiology and Pharmacology for Physicians for the first half of 1966. In his role as President of the Society he was instrumental in moving the publications affairs from the old Board of Publications Trustees to the current Publications Committee, structured to be more responsive to Council decisions. He was a member of the first Education Committee of the Society and with Dr. Hermann Rahn organized the first course for teachers at the Fall Meeting in Madison, Wisconsin in 1954.

"His skills as a teacher have been the envy of many, demonstrating the ease of crystallization of ideas, capability of lecturing to any level of scientific sophistication. His books on the lung and physiology of respiration continue to reflect his skill and knowledge in this area. Dr. Comroe has influenced biomedical research and research training by his distinguished service on many important committees and councils at the national level.

"During the past few years Dr. Comroe has been engaged in a major research project which has been termed 'Project Hindsight,' to define the developments in research that have lead to major clinical advances in the diagnosis and treatment of common diseases of the heart, blood vessels and lungs. This major effort has thus far been reported to the National Institutes of Health and to Congress as a definitive source of information on how advances in medicine are made.

"Dr. Comroe's contributions to education and research have been recognized by several honorary degrees and by other prestigious awards. Time does not permit enumeration of all of these, but mention must be made of the Gold Heart Award of the American Heart Association in 1968 and again in 1973; the Trudeau Award of the American Lung Association in 1974; the Association Of Chairmen of Departments of Physiology Award for outstanding contributions to teaching in 1974; and the Kovalenko Medal of the National Academy of Science in 1976."

Dr. Selkurt stated that it was his great pleasure to add another distinguished award to Dr. Comroe's collection, the Daggs Award of the American Physiological Society.

Dr. Comroe, in accepting the award, stated, "Thank you very much Mr. President and thank you American Physiological Society. I deeply appreciate this award from the American Physiological Society and I am especially pleased that it is the Ray Daggs Award because in my opinion Ray deserves to be honored each year by the Society for his tremendous dedication to the work on the goals of the Society and his many innovations in its scientific meetings, its journals, and educational programs.

"After listening to the Oscar Awards on TV last week, I resolved that I would not acknowledge here today my great debt to my producer, director, choreographer or hairdresser, but I do want very briefly to acknowledge a 40 year old debt to the American Physiological Society. Something was omitted just now from my 'obituary' that the President just read to you and it was probably the most important event in my career. In 1936, after I had served a two-year internship at the University of Pennsylvania, I became instructor in Pharmacology at that school. It really was not a Department of Pharmacology though it was that in name; it was a Department of Physiology with A. N. Richards as Chairman and as its other Professors, Arthur Walker of renal physiology fame, Isaac Starr and Carl Schmidt (later Chairman of the Department).

As an instructor in 1936, I received the salary of $1,800 per year. After a year or two I began to wonder if I would be any good at research or whether I should go back into internal medicine as my brother had before me and my father had before him. What I needed at that time in 1938 was some encouragement and some assurance which most professors were rather reluctant to give and still are reluctant to give to their younger staff members. In March 1938 that encouragement came to me from a letter from the Department of Physiology at Harvard Medical School; the letter was signed by W. B. Cannon. This letter was very short and I would like to read it to you.

March 4, 1938

Dear Dr. Comroe:

With much pleasure I announce that the Committee of the Federation of American Societies for Experimental Biology, charged with the responsibility for arrangements for the International Physiological Congress to be held in Zurich next summer, has selected you as the representative of the American Physiological Society. The fellowship which will be granted you is now $300.00 instead of $250.00 as announced. I am writing to Dr. Fenn, Treasurer of the International Congress fund, to inform him that you have been selected.

Yours sincerely,
W.B. Cannon

"This was extremely important to me because that fellowship from the APS in 1938, telling me that the Society was willing to invest in me what I believe was probably half of its annual operating budget for that year, really committed me to a life time career in physiology. I have never thought of doing anything else since I got that letter from Walter Cannon. The first award in 1938 was a very nice way indeed to start my career and this second award today is a very nice way of your telling me that the $300.00 invested in me in 1938 was not entirely wasted. Thank you very much."

FIRST REVISION OF A HANDBOOK OF PHYSIOLOGY

Later this summer the first volume of the completely revised neurophysiology section of the Handbook of Physiology will be available. The title of the section has been changed to The Nervous System, indicating the greatly enlarged scope of the section.

Cellular Biology of Neurons, edited by Eric R. Kandel, is a systematic introduction to functioning nerve cells. The book is written so as to be useful to a wide readership ranging from graduate students who are beginning to read in neural science to scientists in other fields who want to learn about one or another aspect of neuronal functioning. Each chapter summarizes principles underlying an important and active area of research; the volume is organized to emphasize the scope, the directions, and the excitement of modern cellular neurobiology. An examination of the contents should encourage all physiologists to read the volume.

TABLE OF CONTENTS

Overview – S. W. Kuffler

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General Morphology of Neurons and Neuroglia – Sanford L. Palay and Victoria Chan-Palay

EXCITATION AND CONDUCTION

Core Conductor Theory and Cable Properties of Neurons – Wilfrid Rall

Ionic Basis of Resting and Action Potentials – Bertil Hille

Structural and Metabolic Processes Directly Related to Action Potential Propagation – L. B. Cohen and P. De Weer

Physical Principles and Formalisms of Electrical Excitability – Alan Finkelstein and Alexander Mauro

Activation in Striated Muscle – L. L. Costantin

JUNCTIONAL TRANSMISSION

Structure of the Synapse – J. E. Heuser and T. S. Reese

Junctional Transmission I. Postsynaptic Mechanisms – Akira Takeuchi

Junctional Transmission II. Presynaptic Mechanisms – A. R. Martin

Electrical Transmission: A Functional Analysis and Comparison to Chemical Transmission – M.V.L. Bennett

Junctional Transmission in Smooth Muscle and the Autonomic Nervous System – Mollie E. Holman and G.D.S. Hirst

Biochemistry and Physiology of Cholinergic Transmission – B. Collier

Biochemical Aspects of Neurotransmitter Receptors – A. Maelicke, B. W. Fulpius, and E. Reich

Cellular Aspects of Catecholaminergic Neurons – L. B. Geffen and B. Jarrott

Biochemistry and Physiology of Serotonergic Transmission – Michael D. Gershon

Biochemistry and Physiology of Amino Acid Transmitters – K. Obata

Cellular Biology of the Neurosecretory Neuron – Carol Ann Mason and Howard A. Bern

Axonal Transport: The Intracellular Traffic of the Neuron – Bernice Grafstein

CELLULAR INTERACTIONS

Cell Culture in Neurobiology – Gerald D. Fischbach and Phillip G. Nelson

Trophic Interactions of Neurons – Jean Rosenthal

Specificity of Neurons and Their Interconnections – Alan D. Grinnell

Glial Cells – Richard K. Orkand

SYSTEMS OF NEURONS

Spinal Neurons and Synapses – R. E. Burke and P. Rudomin

The Olfactory Bulb: A Simple System in the Mammalian Brain – Gordon M. Shepherd

The Physiology of Supraspinal Neurons in Mammals – W. Alden Spencer

NEURONS AND INVERTEBRATE BEHAVIOR

Organization of Invertebrate Motor Systems – Donald Kennedy and William J. Davis

Principles in the Organization of Invertebrate Sensory Systems – C.A.G. Wiersma and Joan L.M. Roach

Neuronal Plasticity and the Modification of Behavior – Eric R. Kandel

The number of text pages was so great that they could not be comfortably contained in a single binding. Therefore, Cellular Biology of Neurons is being published as a consecutively paginated, two-book set, with a complete index in each book. There are 746 pages in part 1 and 492 pages in part 2. The combined 1238 pages and 570 figures make this a truly impressive set. It will be available to members of The American Physiological Society at a reduced price when purchased directly from the Subscription Office, American Physiological Society, 9650 Rockville Pike, Bethesda, Maryland 20014.

The Section Editors, John M. Brookhart and Vernon B. Mountcastle, have selected the Editors for the next two volumes in the section. Editors and authors are actively at work preparing these volumes. Ian Darian-Smith is editing the volume on sensory processes and Vernon B. Brooks is editing the volume on motor functions.

HONORS AND AWARDS

Dr. Morris Rockstein, Professor of Physiology and Biophysics at the University of Miami, as an honored alumni of the University of Minnesota, was presented with an outstanding achievement award by C. Peter Magrath, President of the University of Minnesota. Dr. Rockstein, an APS member, is a pioneer in the study of biochemical aspects of aging of organisms; leader in research in insect physiology and biochemistry and the whole field of gerontology. He is a noted author and editor of several scholarly works, including the standard reference, The Physiology of Insects.

Dr. Christian J. Lambertsen, University of Pennsylvania, Philadelphia, was elected to membership in the National Academy of Engineering for contributions to environmental science and to diving physiology and technology.

APS Fall Scientific Meeting

October 9-14, 1977

Diplomat Resort and Country Clubs Hollywood, Florida

SCIENTIFIC PROGRAM

Scientific sessions will be scheduled from 9 a.m. to 4:30 p.m. Monday through Friday, with the exception of Wednesday afternoon. Each half-day period will consist of one symposium and simultaneous sessions of volunteer papers presented either in slide or poster sessions. The Bowditch Lecture will take place on Tuesday and the Society Business Meeting will be held on Thursday.

Tutorial Lectures

Non-invasive techniques for measurement of pulmonary blood flow: A review. L.E. FARHI, SUNY Buffalo Sch. of Med.

Gravitational physiology. A.H. SMITH, UC, Davis

Local regulation of blood flow. R.H. BERNE, Univ. of Virginia Med. Sch.

The gramicidin channel. PETER LAUGER, Univ. of Konstanz, West Germany

Lithium, membranes and manic-depressive illness. A cure in search of a disease. J.M. DIAMOND, UCLA

Albumin synthesis and secretion. THEODORE PETERS, JR., Mary Imogene Basset Hosp.

Alpha-adrenergic control of glycogen metabolism. J.H. EXTON, Vanderbilt Univ., Sch. of Med.

Glycolytic control mechanisms in aerobic and ischemic heart muscle, J.R. NEELY, Penn State Univ., Hershey Med. Ctr.

Four additional Tutorial Lectures will be announced in the Program.

Symposia

October 10 — Monday

AM — PROXIMAL TUBULAR FUNCTION IN HEALTH & DISEASE

Co-Chairmen: L. A. Bricker, U. Miami
T. E. Andreoli, U. Alabama

Speakers: J. A. Schafer, U. Alabama
D. J. Marsh, U.C.L.A.
R. Gilbert, Montefiore Hosp.
M. B. Burg, N.I.H.

PM — DISTAL NEPHRON FUNCTION IN HEALTH & DISEASE

Co-Chairmen: T. E. Andreoli, U. Alabama
L. A. Bricker, U. Miami

Speakers: D. Warnock, U.C.L.A.
V. Dennis, Duke U.
R. Kaplan, U. Miami
J. P. Kokko, U. Texas

October 11 — Tuesday

AM — MEMBRANE CHANNELS I

Chairman: W. R. Loewenstein, U. Miami

Speakers: J. M. Diamond, U.C.L.A.
W. R. Loewenstein, U. Miami
P. Lauger, U. Konstanz
D. A. Hayson, Cambridge U.

PM — MEMBRANE CHANNELS II

Chairman: P. Lauger
U. Konstanz, West Germany

Speakers: F. Bezanilla, U.C.L.A.
C. Stevens, Yale U.
B. Sackmann, Max-Planck, Inst. Göttingen
M. Raftery, U.C.L.A.

October 12 — Wednesday

AM — PULMONARY CIRCULATION

Chairman: A. B. Otis, Gainesville, U. Florida

Speakers: J. Gil, U. Miami
G. Pietra, U. Pennsylvania
E. Schneeberger, Harvard U.

AM — MECHANISMS OF TRANSMITTER RELEASE: A COMPARISON OF PHYSIOLOGICAL, STATISTICAL AND MORPHOLOGICAL FINDINGS

Chairman: K. L. Magleby, U. Miami

Speakers: T. S. Reese, N.I.H.
R. L. Volle, U. Connecticut
K. L. Magleby, U. Miami

October 13 — Thursday

AM — PHYSIOLOGY AND PHARMACOLOGY OF CORONARY CIRCULATION

Co-Chairmen: R. M. Berne, U. Virginia
P. Somani, U. Miami

Speakers: R. M. Berne, U. Virginia
P. J. Kadowitz, Tulane U.
J. I. E. Hoffman, Calif. UCSF
P. Somani, U. Miami

PM — THE PHYSIOLOGICAL BASIS OF MENTAL FUNCTIONS

Chairman: D. L. Wilson, U. Miami

Speakers: N. Geschwind, Harvard U.
K. Pribram, Stanford U.
D. L. Wilson, U. Miami
S. S. Kety, Harvard U.

October 14 — Friday

AM — B ADRENERGIC RECEPTORS

Chairman: L. Potter, U. Miami
Speakers: R. Lefkowitz, Duke U.
P. Molinoff, U. Denver
A. Gilman, U. Virginia
M. Schramm, U. Jerusalem

PM — DEVELOPMENTAL SIGNALLING IN THE NERVOUS SYSTEM

Chairman: M. Jacobson, U. Miami
Speakers: R. K. Hunt, Johns Hopkins U.
J. Diamond, McMaster U.
M. Jacobson, U. Miami

PM and Evening October 12 — Wednesday

Refresher Course

MECHANISMS AND REGULATION OF GASTROINTESTINAL SECRETION AND ABSORPTION

I. Mechanisms of Secretion. George Sachs, U. Alabama
II. Mechanisms of Absorption. S. G. Schultz, U. Pittsburgh
III. Gastrointestinal Endocrinology. L. R. Johnson, U. Texas
IV. Regulation of Gastric and Pancreatic Secretion. L. R. Johnson, U. Texas

REPORT FROM THE SECTION ON NEUROPHYSIOLOGY

The Section on Neurophysiology was established in 1974 in order to implement the recommendations of the Task Force on Neurophysiology, published in the Physiologist 17:139:1974. The purpose of the Section on Neurophysiology was to create a committee responsible for coordinating and organizing activities for neurophysiologists within the APS and in particular, to advise the program committee on neurophysiology-related symposia and activities for the FASEB Spring Meeting. This function has assumed progressively greater importance as participation by neurophysiologists within the APS has dramatically declined the last several years, due at least in part to the fact that almost every neurophysiologist is an active participant in the Society for Neuroscience. The Section on Neurophysiology does not feel that it is either necessary or appropriate to compete with the Society of Neuroscience, which serves a very important function in providing meetings geared to a multidisciplinary approach to the study of the nervous system. However, neurophysiology also belongs within the APS, both as a self-contained subgroup of physiology and in its interactions with physiology of other organ systems. The Spring FASEB Meeting occurs at a different place and time of year than the fall meetings of the Society for Neuroscience, and provides an important opportunity for junior neurophysiologists to gain experience in presenting papers as well as an opportunity for more established persons to communicate and interact. One major function of the steering committee is to make the Spring FASEB Meetings more attractive to neurophysiologists.

In the past the steering committee of the Section on Neurophysiology has been appointed. In an effort to formalize the steering committee and to make it more representative of the neurophysiologist members of the APS, the committee in the future will consist of nine elected members with three members elected each year for a three year term. To accomplish this and still provide continuity, six members of the past steering committee will be retained for one or two year terms and three new members will be elected from six names submitted for nomination. The members and nominees for election to the steering committee are listed below.

Members to Rotate after 1 year:

Kiyomi Koizumi, M.D. Department of Physiology, Downstate Medical Center, Brooklyn, N.Y. 11203

Phillip Nelson, Ph.D., M.D. Behavioral Biology Branch, National Institute of Child Health and Human Development, Bethesda, MD 20014

Lloyd Partridge, Ph.D. Department of Physiology and Biophysics, University of Tennessee, Memphis, TN 38103

Members to Rotate after 2 years:

David O. Carpenter, M.D. Neurobiology Department, Armed Forces Radiobiology Research Institute, Bethesda, MD 20014

Donald Humphrey, Ph.D. Department of Physiology, Emory University, Atlanta, GA 30322

Dennis Poulos, Ph.D. Department of Physiology and Neurosurgery, Albany Medical College, Albany, N.Y. 12208

Candidates for Election to the Neurophysiology Steering Committee:

Charles Edwards, Ph.D. State University of New York, Albany, N.Y. 12222

Barbara G. Gordon-Lickey, Ph.D. Psychology Department, University of Oregon, Eugene, OR 97403

Henry J. Ralston, Ph.D. Department of Physiology, School of Dentistry, University of the Pacific, San Francisco, CA 94115

Forrest Weight, M.D. National Institute of Mental Health, St. Elizabeth's Hospital, Washington, D.C. 20032

William D. Willis, Jr., M.D. Marine Biomedical Institute, Galveston, TX 77550

Clinton Woolsey, M.D. Waisman Center, University of Wisconsin, Madison, WI 53706

Ballots will be mailed to all APS members who have indicated an interest in neurophysiology in the late summer. Anyone not receiving such a ballot by 1 September 1977 should contact the APS office. One of the first duties of the new steering committee of the Section on Neurophysiology will be to prepare a statement of organization and procedures for submission to the APS Council in order to formalize this Section. Suggestions as to neurophysiology related programs for the Spring Meetings may be given to any member of this committee.

INSTRUCTIONS FOR APPLYING FOR APS MEMBERSHIP

At the April 1977 business meeting the proposed Bylaws Amendment for creating a new membership category for Students was passed. This Bylaw Amendment appears under Section 7 of Article III of the Constitution, printed below.

CURRENT APPLICATION FORMS

Starting with this issue, The Physiologist shall routinely carry one copy of the current application form (following). This form will serve for all categories of membership. Any member desiring to sponsor more than one applicant may use a Xerox copy of this form. Any application submitted on an out-dated form will be returned to the sponsor to be redone on the acceptable form.

One application form serves all membership categories. There are, however, specific sets of instructions for each category. Therefore it is essential that sponsors and applicants carefully attend to those instructions specific to their desired category.

GENERAL INSTRUCTIONS

FOR ALL CATEGORIES:

Use only the current application form. Check the box indicating the category of membership for which you are applying. Use the SPECIAL INSTRUCTIONS for that category when filling out the form. Type the Application. Fill out all applicable spaces. Only completed applications will be reviewed.

The Bibliography must be submitted in the form found in the Society's journals. An example of the correct form is:

JONES, A.B., and C.D. Smith. Effect of organic ions on the neuromuscular junction in the frog. Am. J. Physiol. 220:110, 1970.

Send no reprints.

Deadline Dates: Completed applications received between February 1 and July 1 are considered for nomination by the Council at the Fall Meeting. Applications received between July 1 and February 1 are considered for nomination by the Council at the Spring Meeting. Applications are not complete until all materials, including sponsor's letters, are received.

QUALIFICATIONS (Except Students):

The Membership Advisory Committee uses the following 5 categories in evaluating an application:

1. Educational History. Academic degree and postdoctoral training are evaluated and assessed with regard to how closely the applicant's training has been tied to physiology.

2. Occupational History. Particular emphasis is given to those applicants who have a full time position in a department of physiology, or are responsible for physiology in another department. Relatively high ratings are given to people with positions in clinical departments and to people functioning as independent investigators in commercial or government laboratories.

3. Contributions to the Physiological Literature. This category is of major importance. The applicant's bibliography is evaluated on the basis of publications in major, refereed journals which are concerned with problems judged to be primarily physiological in nature. Emphasis is given to papers published as the result of independent research. Special note is taken of publications on which the applicant is sole author or first author.

4. Interest in and Commitment to Teaching Physiology. This evaluation is based on: (1) the fraction of the applicant's time devoted to teaching, (2) publications related to activities as a teacher including production of educational materials, and (3) special awards or other recognition the applicant has received for outstanding teaching effectiveness.

5. Special Considerations. This category permits the Membership Advisory Committee to acknowledge unique accomplishments of an applicant. These might be excellence in a specific area, or unusual contributions to Physiology resulting from talents, interest or a background substantially different from the average.

SPONSORS:

Primary responsibility for membership rests with the two sponsors who must be regular members of the Society. Sponsors should discuss the appropriateness of the selected category of membership in this Society with prospective applicants.

Each sponsor should write an independent confidential letter about the candidate using the five categories listed above to evaluate the candidate.

CHECK LIST:

1. Original copy of application signed by both sponsors.
2. Application on a current form, including the bibliography (1 original and 7 copies).
3. Mail the original, which has been signed by the two sponsors, plus 7 copies to:

Executive Secretary
American Physiological Society
9650 Rockville Pike
Bethesda, Maryland 20014

SPECIAL INFORMATION AND INSTRUCTIONS

FOR REGULAR MEMBERSHIP

Bylaws of the Society:

Article III, Section 2 - Regular Members. Any person who had conducted and published meritorious original research in physiology, who is presently engaged in physiological work, and who is a resident of North America shall be eligible for proposal for regular membership in the Society.

IF ALIEN: Please attach a letter and 7 copies stating visa status and type of passport and giving evidence of intent to stay in North America.

Duties and Privileges:

1. Hold Elective Office.
2. Vote at Society Meetings.
3. Serve on Committees, Boards and task forces.
4. Serve on Federation Boards and Committees.
5. Sponsor New Members.
6. Orally present or co-author a contributed paper and sponsor a non-member authored paper at the Fall scientific meeting.
7. Orally present or co-author one contributed scientific paper at the annual Federation meeting or sponsor one paper.
8. Receive the Society publications, The Physiologist and The Physiology Teacher.
9. Receive Federation Proceedings.
10. Subscribe to handbooks and periodicals published by the Society at membership rates.
11. Register to attend scientific meetings of the Federation and the APS Fall meeting at membership rates.
12. Participate in FASEB Member's Life Insurance Program, Disability Program and in Hospital Protection Plan. (For Residents of the United States, its territories or possessions).
13. Eligible to receive the Daggs Award.
14. Eligible to be selected as Bowditch Lecturer (members under 40 years of age).

FOR CORRESPONDING MEMBERSHIP

Bylaws of the Society:

Article III, Section 3 - Corresponding Members. Any person who has conducted and published meritorious research in physiology, who is presently engaged in physiological work and who resides outside of North America shall be eligible for proposal for corresponding membership in the Society.

Duties and Privileges:

1. Serve on Society Committees, Boards and Task Forces.
2. Serve as one sponsor of new Corresponding Members (One regular member must be sponsor of a new Corresponding Member).
3. Orally present or co-author a contributed paper and sponsor a non-member authored paper at the Fall scientific meeting.
4. Orally present or co-author one contributed scientific paper at the annual Federation meeting or sponsor one paper.
5. Receive the Society publications, The Physiologist and The Physiology Teacher.
6. Receive Federation Proceedings.
7. Subscribe to handbooks and periodicals published by the Society at membership rates.
8. Register to attend scientific meetings of the Federation at membership rates.

FOR ASSOCIATE MEMBERSHIP

Bylaws of the Society:

Article III, Section 5 - Associate Members. Persons who are engaged in research in physiology or related fields and/or teaching physiology shall be eligible for proposal for associate membership in the Society provided they are residents of North America. Associate members may later be proposed for regular membership.

Duties and Privileges:

Same as for Regular Members except for the privilege of:

1. Holding Executive Office, or membership on certain committees.
2. Voting at Society Meetings.
3. Sponsoring New Members.
4. Receiving the Daggs Award.
5. Selection as Bowditch Lecturer.

FOR STUDENT MEMBERSHIP

Not all questions on the application form may be appropriate – Please place NA next to any such question.

Bylaws of the Society:

Article III, Section 7 - Student Members. Graduate students in physiology who have completed their preliminary examinations for the doctoral degree provided they are residents of North America. No individual may remain in this category for more than five years.

Duties and Privileges:

1. Present one contributed paper at the Fall Scientific meeting with the endorsement of the student's advisor.
2. Receive the Society publications, The Physiologist and The Physiology Teacher.
3. Subscribe to Handbooks and Periodicals.
4. Register to attend scientific meetings of the Federation and the APS Fall meeting at student rates.

This Form is Valid Only for 1978

APPLICANT'S LAST NAME _____

Date _____

THE AMERICAN PHYSIOLOGICAL SOCIETY

9650 Rockville Pike, Bethesda, MD 20014

MEMBERSHIP APPLICATION FOR:

REGULAR ☐
CORRESPONDING ☐
ASSOCIATE ☐
STUDENT ☐

CURRENT MEMBERSHIP CATEGORY; YEAR ELECTED _____

See Instructions

Name of Applicant: _____
First Middle Last

Mailing Address _____ Birth Date: _____

Citizenship: _____

Country of Permanent Residence: _____

Telephone No.: _____
Zip Code

1. **EDUCATIONAL HISTORY** (Predoctoral students indicate date preliminary examination was passed.)

Dates	Degree	Institution	Major Field	Advisor

Doctoral Dissertation Title: (if any)

Postdoctoral Research Topic:

2. **OCCUPATIONAL HISTORY**

Present Position:

Prior Positions:

Dates	Title	Institution	Department	Supervisor

SPONSORS

#1. Name: _____

Mailing Address: _____

Telephone No. Zip Code

#2. Name: _____

Mailing Address: _____

Telephone No. Zip Code

I have read the guidelines for applicants and sponsors and this application and attest that the applicant is qualified for membership.

#1 Signature _____ #2 Signature _____

Each sponsor must submit an original and 7 copies of a confidential letter of recommendation to the Society, under separate cover.

APPLICANT'S LAST NAME _____

3. **DESCRIBE YOUR PHYSIOLOGICAL TEACHING** – What percent of your time/effort is spent in teaching Physiology?_____

Describe in the space provided your teaching of physiology including course descriptions (content, format); supervision of pre-doctoral and post-doctoral students; special contributions (films, textbooks, etc.).

4. **INTEREST IN THE SOCIETY** – List any APS Meetings attended by date and check the appropriate box for any papers.

SPRING (FASEB)

Date	Presented	Coauthor
_____	☐	☐
_____	☐	☐
_____	☐	☐
_____	☐	☐
_____	☐	☐

FALL (APS)

Date	Presented	Coauthor
_____	☐	☐
_____	☐	☐
_____	☐	☐
_____	☐	☐
_____	☐	☐

List other scientific societies of which candidate is a member:

In the space provided state your interest in wanting to join the Society:

5. **SPECIAL CONSIDERATION** – Include any other contributions (Administrative, university, national service, awards and honors) that may be important to physiology.

6. **DESCRIBE YOUR RESEARCH** – What percent of your time/effort is spent in research?_____

Describe the fundamental physiologic questions in your research and how you have answered these questions. Limit the paragraph to the space provided.

7. **BIBLIOGRAPHY** – Attach a list of your publications under the following categories:
   1. Complete physiological papers, published or accepted for publication.
   2. Physiological abstracts (limit to ½ page).
   3. Other papers not primarily physiological (limit to ½ page).

The entire bibliography should not exceed 2 pages. Give complete titles and journal references with inclusive pagination. Use the bibliographic form found in the Society's journals. List authors in the order in which they appear in the publication.

COUNCIL OF ACADEMIC SOCIETIES BRIEF

ASSOCIATION OF AMERICAN MEDICAL COLLEGES • 1 DUPONT CIRCLE NW • WASHINGTON DC
(202) 466-5100 SPRING, 1977 VOL. 2, NO. 3

HEALTH MANPOWER ACT. The Health Professions Educational Assistance Act of 1976 (P.L. 49-484) was signed by President Ford on October 12, 1976. Implementing regulations have developed slowly, in part because of the complexity of the law and in part because of the cumbersomeness of the DHEW regulation review procedures. In addition to the usual assurances of first-year enrollment levels and institutional nonfederal expenditures, capitation funding hinges on requirements in the two areas described as follows:

Primary care residency positions. Effective July 15, 1977, 35% of all filled residency positions must be in the primary care specialities of internal medicine, pediatrics, and family medicine in those programs operated in facilities that are either owned by or affiliated with medical schools. If a position was filled in 1976 by a resident who is no longer in a primary care residency, that position will be discounted from the total primary care count.

Major concerns surround the definition of an affiliated program and the nonprimary care positions. The Department's proposals for these will be published in a Notice of Intent of Proposed Rule Making to be released in May.

If the 35% proportion is not met in the July 1977 count, all schools seeking capitation will have to have a 40% proportion in primary care in 1978 and a 50% proportion in 1979. At present, available data from AAMC and from the National Intern and Residency Matching Plan (NIRMP) indicate that the 35% national level will be met in 1977.

U.S. students in foreign medical schools. In the academic year 1978, medical schools will be required to reserve a number of places sufficient for the transfer into the second-, third-, or fourth-year classes of U.S. citizens who were enrolled in foreign schools prior to October 12, 1976. These transferring students must have successfully completed two years of study and must have passed Part I of the National Board of Medical Examiners (NBME).

Implementation of this provision is extremely complex. The problems of identifying eligible students, apportioning positions among the schools on the basis of enrollment, and facilitating the application to schools by students are complicated by the fact that some schools may not participate at all in the capitation, and others may request and receive waivers from this provision. At present, the Bureau of Health Manpower hopes to have applications for students to send to the Secretary in the mails by June 1, but the Office of Management and Budget must clear these forms.

Upon receiving the application forms, students will find they must get their foreign schools to send a transcript and an affidavit stating that they have successfully completed two years of study. Obtaining these documents from many foreign schools may be difficult. At present, the Bureau of Health Manpower is considering developing a matching program. Such a program would assist both the students in their search for a place and the schools in demonstrating that they have made a good-faith effort to fill their reserved positions.

Special projects. The Act authorizes support of residency programs in general internal medicine and general pediatrics through grants or contracts. Application materials for these projects were sent to every medical school dean's office on April 15. The deadline for receipt of completed applications by HRA is May 30.

Foreign medical graduates. The law returns the Exchange Visitor Program to its original intent--that foreign physicians be educated in U.S. institutions in order that they may serve their own countries' needs. Future graduates of medical schools not accredited by the Liaison Committee on Medical Education who come to the U.S. to participate in programs involving patient care must have their programs arranged between governmental agencies or institutions in their countries of origin and U.S. medical schools and their hospitals. The physician must pass Parts I and II of the National Board (or its equivalent). The NBME will give this exam on September 7-8, 1977, in 20 locations throughout the world.

It is expected that by 1978 the number of foreign medical graduates entering U.S. programs in graduate medical education will be reduced to a trickle. Meanwhile, the number of U.S. graduates is rising. Approximately 13,800 will graduate this year.

FY 1978 APPROPRIATIONS. Federal appropriations for FY 78 are now being established. The ceiling set by Congressional Budget committees will probably be about $8 billion for all health funds other than Medicare-Medicaid. This is $1.1 billion below the recommendations of the Coalition for Health Funding (CHF). This constraint will seriously jeopardize attaining the CHF recommendations for NIH, ADAMHA, and the Health Resources Administration. The comparative dollar figures are as indicated in the following table:

	Administration Budget Request	Coalition for Health Funding Budget Recommendations
NIH	$2.576 billion	$3.070 billion
ADAMHA	.947 billion	1.101 billion
HRA	.588 billion	1.250 billion

The significant increase in HRA appropriations is needed to implement the provisions of P.L. 94-484.

Adequate funding for research and education is increasingly difficult to achieve in a climate in which the emphasis is on the containment of health costs. Members of the academic community must explain to their Congressmen that the nation's efforts in research and education are long-term investments. Short-term strategies to contain expenditures on health services must not cripple programs in research and education which, in the future, can significantly improve health status.

H.R. 2222. This bill, which would direct the NLRB to define housestaff as employees, is still in the House Subcommittee on Labor-Management Relations. It is important that the views of faculty and housestaff who oppose this bill be made known to Frank Thompson, Chairman of the House Subcommittee on Labor-Management Relations, and Carl D. Perkins, Chairman of the House Committee on Education and Labor.

The CAS Brief is prepared by the staff of the AAMC's Council of Academic Societies and is distributed through the auspices of your member society.

THE PHYSIOLOGICAL BASIS OF CIRCADIAN TIMEKEEPING IN PRIMATES*

Martin C. Moore-Ede
and
Frank M. Sulzman
Department of Physiology
Harvard Medical School
Boston, MA 02115

Organisms ranging from unicellular algae (12) to man (2) demonstrate the capability to measure approximately twenty-four hour intervals of time. The circadian timing system within the organism thereby allows the prediction of events which are well correlated with the twenty-four period of the earth's rotation. In particular, it appears to be of survival advantage to predict the day-night patterns of predator activity, food availability and environmental conditions. To this end many behavioral and physiological functions have a highly organized temporal structure which is most obviously recognized as the circadian rhythmicity of physiological variables.

While the formal properties of the circadian timing system have been extensively described, relatively little is known about the physiological basis for circadian time measurement. In the large part, previous investigators have concerned themselves with what are essentially "black-box" properties of circadian timekeeping mechanisms. Diagramatically represented in Figure 1, the black-box represents the organism which generates spontaneous circadian rhythms in many behavioral and physiological outputs. These outputs are normally synchronized to oscillating inputs from the environment, termed "zeitgebers," the most prominent example of which is the twenty-four hour light-dark cycle. However, we know the black-box, or organism, is a spontaneously oscillating system, since when it is placed in an environment free of periodic environmental inputs it still continues to generate circadian rhythms. These rhythms are, however, no longer synchronized to a precise twenty-four hour period, but instead free-run with periods which are close to, but usually significantly different from twenty-four hours. Over the last twenty years, the characteristics of entrainment by zeitgebers, the differential sensitivity of the circadian system at various phases of the circadian cycle described by phase-response curves, the temperature compensation of the system so that it is protected against environmental temperature changes, and the physical, chemical and genetic factors which determine the spontaneous free-running period have all been extensively studied and multiply reviewed (3,10,13,15).

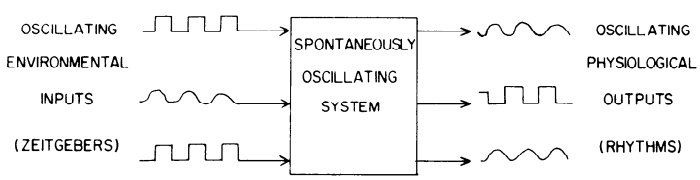

Fig. 1. Most investigations to date have considered the circadian timing system as a "black-box" and have been concerned with describing the formal properties of the system. This review is concerned with the anatomy and physiology of the elements within the black-box.

*Taken from the introductory remarks given by Dr. Moore-Ede at the session on Chronobiology & Biological Rhythms at the 1977 Federation Meetings.

The time has come to determine the anatomy and physiology of the system within the black-box. In this review we will discuss work from our laboratory which is attempting to answer a number of key questions. We wish to know a) whether there are one or many oscillators or "clocks" within the system, b) where the oscillators are anatomically located within the organism, c) if there are multiple oscillators, how do they communicate with each other so that the internal synchronization within the system is maintained, d) what are the physiological elements which are involved in the exteroception of temporal cues from the environment and the conveyance of this information to the endogenous oscillators, and e) what are the mechanisms by which the circadian oscillators time physiological events. Finally, we are interested in what happens when the circadian timing system is disturbed by pathophysiological processes and the consequences this has for human health and disease.

Models of the Circadian Timing System

With so little known about the anatomical and physiological organization of the circadian timing system, we decided that it would be worthwhile to state explicitly the various possible modes of physiological organization which could account for the known properties of the system. Our aim was to provide formalized descriptions of possible organizations which would aid in the focusing of experimental designs to test the key theoretical alternatives. The models we developed had to be compatible with the known formal properties of the circadian timing system. In particular we had to account for the external synchronization with environmental time cues, and the internal synchronization of the various circadian rhythms within the organism whether or not the system was externally synchronized.

The three alternative models of the circadian timing system which we have developed (21) are presented in Figure 2. Although many intermediate possibilities exist, we believe these three abstract models summarize most distinctly the various possible types of organization of the circadian timing system. Each model represents the tissues of the animal (A,B,C, etc.) as either active elements ⊜ which can spontaneously generate circadian rhythms in the absence of any periodic input, or passive elements (□) which may passively follow a forcing periodic input, but cannot by themselves generate spontaneous circadian rhythms. Temporal communication between the tissues of the animal (primarily hormonal or neural) is represented by the rhythmic outputs (~) labelled a,b,c, etc. We, of course, recognise that a given tissue or even cell may have both active and passive elements which determine its output. However, we consider a tissue as containing an oscillator if a statistically significant component of its output is determined by an active circadian element.

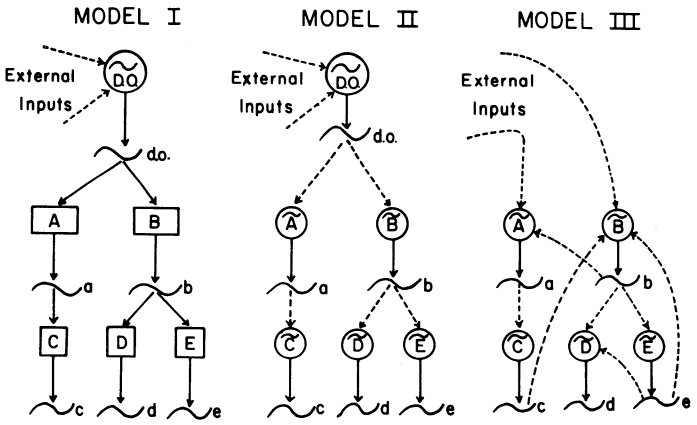

Fig. 2. Three alternative models of the mammalian circadian timing system. The symbol ⊙ represents an active cellular unit capable of maintaining a self-sustained oscillation with its own independent period; □ represents a cellular unit that responds passively to an oscillating driving force; ~ indicates the oscillating concentration of a chemical mediator; ⇢ indicates the entrainment of a self-sustained oscillator by a phase-response mechanism; and → is the direction of flow of passive responses to an oscillating driving force. Model I is therefore a single oscillator system whereas the other models are multioscillator systems arranged in a hierarchical (Model II) or non-hierarchical (Model III) manner.

Thus Model I is a single oscillator system. Here only one tissue or group of cells in the organism (labelled "D.O." for driving oscillator) can generate spontaneous circadian oscillations in the absence of periodic input. The other tissues in the organism (A,B,C, etc.) which display circadian rhythms (a,b,c, etc.) are therefore passively following forcing outputs from the single driving oscillator.

The other two models represent systems in which there are multiple tissues within the organism which can each spontaneously generate circadian rhythms in their own right. In Model II these are arranged in a hierarchical manner with one oscillator (D.O.) acting as a pacemaker which maintains internal synchrony within the system. In contrast, in Model III the multiple oscillators are arranged in a non-hierarchical manner so that internal synchronization is achieved through mutual interaction and coupling between the oscillators. No single oscillator consistently acts as a pacemaker.

The Chair-Acclimatized Squirrel Monkey

Most of the experiments which will be described here were conducted using a chair-acclimatized squirrel monkey preparation. The methodological details have been published previously (19,20), but the main features of the techniques are summarized in Figure 3. Squirrel monkeys are carefully conditioned to accept chair-restraint so that they will maintain body weight and eat normally during experiments lasting up to three weeks in length. During the experiments the animals sit in the metabolism chair within an isolation chamber in which lighting, temperature, and sound cues can be controlled. Patterns of food intake, drinking, activity, body temperature, and urinary potassium, sodium and water excretion are routinely monitored. Additionally, for certain experiments, animals are chronically implanted with arterial and venous catheters several months before, and during the experiments the catheter tubing is extended outside the isolation chamber. Through this tubing it is possible to draw blood samples without disturbing the animal and to administer infusions of hormones or drugs without providing any other temporal cues such as might be induced by opening the chamber or handling the animal. Once suitably conditioned the animals tolerate these experiments very well and show no ill effects.

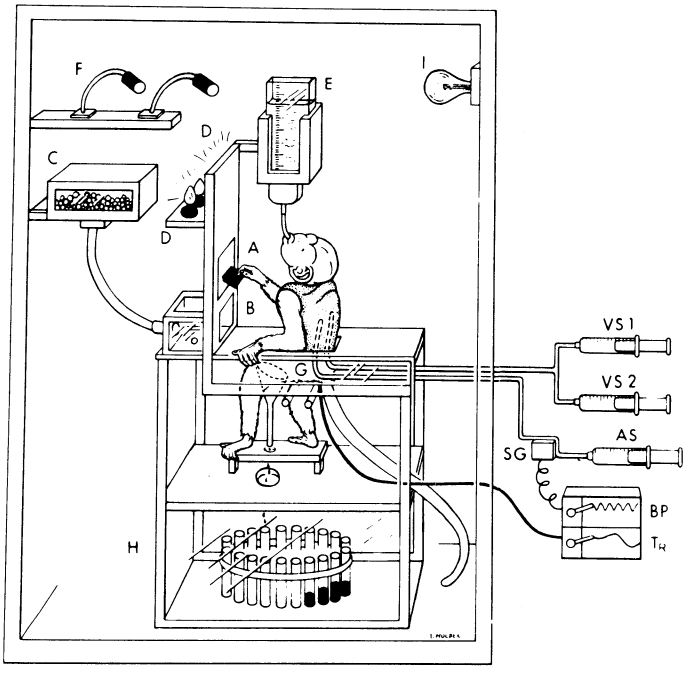

Fig. 3. Chair-acclimatized squirrel monkey within isolation chamber. The monkey operates the lever (A) to gain food pellets (B), and water is available from a bottle (E). Urine is collected from a soft rubber funnel (G) and passes to a fraction collector (H), which can be accessed without disturbing the monkey. The animal's activity is monitored using an ultrasound meter (F). Chronically implanted arterial and venous catheters are led outside the chamber. Venous administration of substances can be pre-programmed using two venous syringes (VS 1&2) powered by Harvard infusion pumps. From the arterial line blood samples can be drawn (AS) and blood pressure monitored via Statham gauge (SG). Rectal temperature (T_a) can also be monitored by a probe.

An example of some data obtained from this squirrel monkey preparation is shown in Figure 4 (20). During the first day, prominent twenty-four hour rhythms (mean ± SEM for four monkeys) were shown in activity, feeding, drinking, and urinary potassium, sodium and water excretion, each rhythm showing a maximum during the lights-on portion of the day. That each of these rhythms is not directly dependent on the light-dark cycle is illustrated by the data in the subsequent days when first the animal was exposed to thirty-six hours of dark (so the lights were not switched on on Day 2) and then exposed to thirty-six hours of constant light (so that lights did not go off on the night portion of Day 4). Throughout these manipulations of the light-dark cycle each of the circadian rhythms persisted with a similar waveform. Such persistence of circadian rhythms in the squirrel monkey in constant environmental conditions (LL: 600 lux) has been demonstrated by us over periods of up to three weeks in the chair-acclimatized monkey and for up to six months in monkeys free-ranging in a cage. Because of such experiments we may define each of these observed rhythms as "circadian" since they persist and free-run with periods significantly different from twenty-four hours when the time cues which normally synchronize them are removed from the environment.

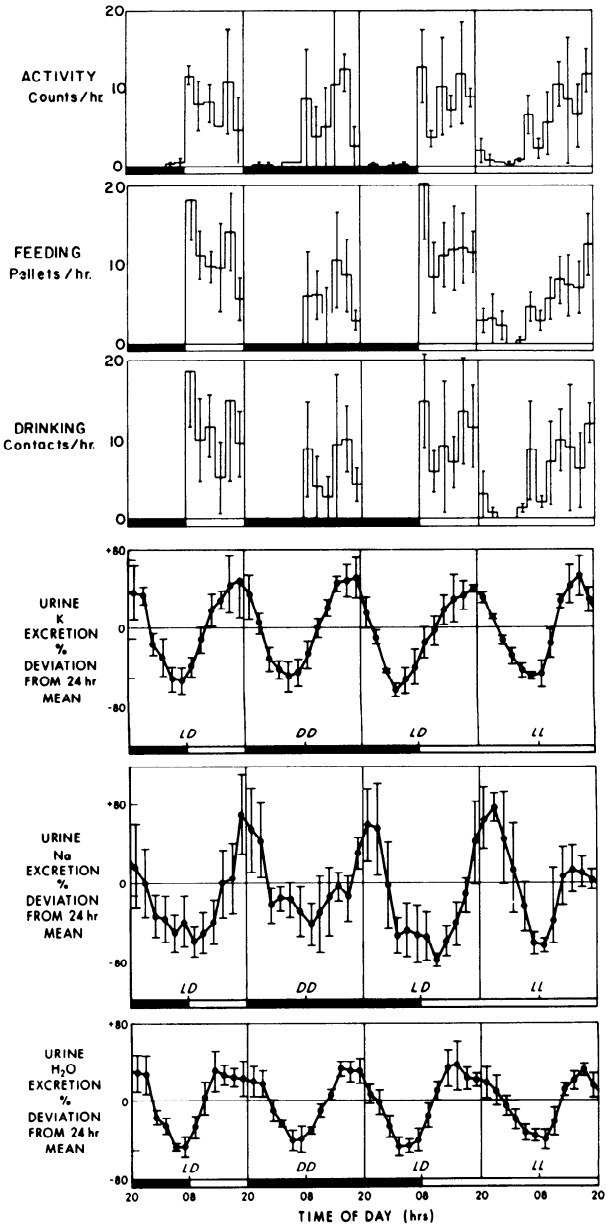

Fig. 4. Circadian rhythms (mean ± SEM) of activity, feeding, drinking and urinary potassium, sodium and water excretion in four squirrel monkeys. After two equilibration days (not shown on the graph) with lights on from 08:00 – 20:00 hr daily, the animals were studied for a control day on the same light-dark cycle followed by a thirty-six hour period of constant darkness and then a thirty-six hour period of constant light. Despite the manipulations of the light-dark cycle each monitored circadian rhythm persisted with a period of approximately twenty-four hours.

Single Versus Multiple Oscillator Systems

A key distinction between single and multioscillator systems is that one should be able to uncouple a multioscillator system and demonstrate independency of different circadian rhythms within an animal, whereas this would be impossible if the organism possessed only a single circadian oscillator.

We have used two main strategies in attempts to internally desynchronize circadian rhythms in the squirrel monkey. Firstly, we have abruptly phase-shifted the light-dark cycle, the major environmental time cue in the squirrel monkey, and examined whether different rhythmic variables within the same animal resynchronized to the new light-dark cycle phase at different rates (20). Figure 5 shows the data from one of these experiments in a monkey in which the light-dark cycle was phase delayed by eight hours. Each of the monitored rhythmic variables gradually resynchronized with the new light-dark cycle phase within approximately one week. However, an examination of the rate of phase shift of each variable (Figure 6) demonstrated that the circadian rhythms of feeding, drinking, activity and body temperature resynchronized significantly more rapidly to the new light-dark cycles phase than did the rhythms of urinary potassium, sodium and water excretion. Thus, we were able to demonstrate a "transient internal desynchronization" of circadian rhythms in the squirrel monkey.

This evidence alone, however, is not sufficient to prove that the circadian timing system is composed of multiple oscillators in the squirrel monkey. It is entirely possible to postulate a Model I type of single oscillator organization with delays built into the system so that some rhythmic functions reset more rapidly than others. Much more conclusive proof would be if one could demonstrate oscillators free-running with quite different periods within the same animal for a sufficient length of time so that they would entirely overlap each other thus realizing all possible phase relationships between the different rhythms.

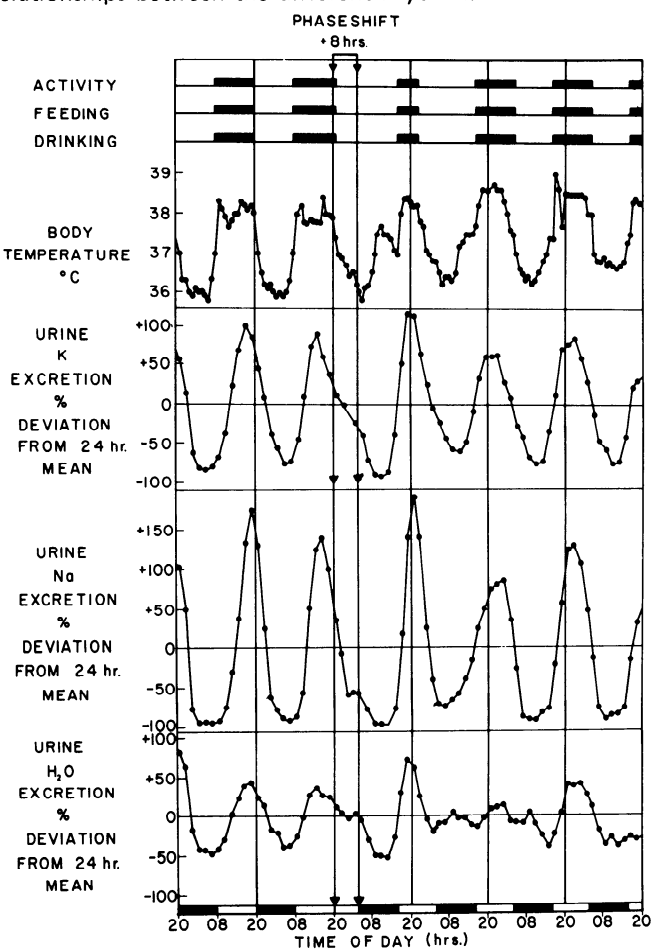

Fig. 5. The response of a monkey to an eight-hour phase-delay of the light-dark cycle. The circadian rhythms of activity, feeding, drinking, body temperature, and urinary potassium, sodium and water excretion are plotted during two control days with lights on from 08:00 – 20:00 hr, and then for the first four days after the light-dark cycle phaseshift where lights were on from 16:00 – 04:00 hr daily. Each circadian rhythm gradually resynchronized with the new light-dark cycle phase.

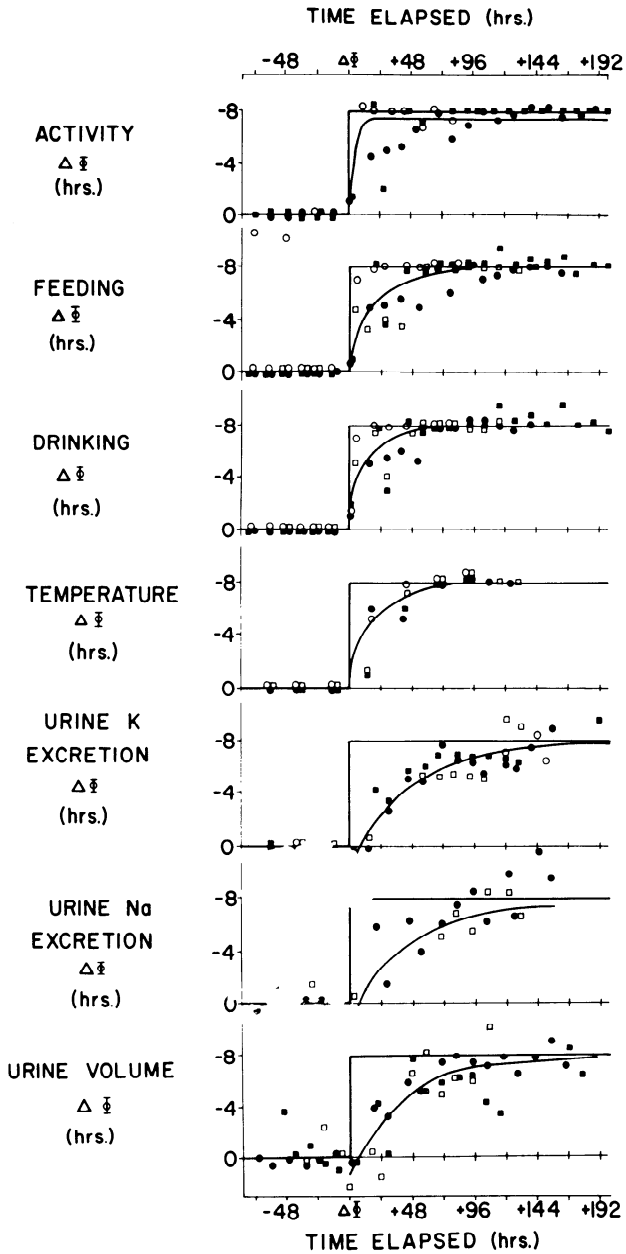

Fig. 6. Response of the circadian rhythms of activity, feeding, drinking, body temperature, and urinary potassium, sodium and water excretion in four squirrel monkeys to an eight-hour phase-delay of the light-dark cycle. The change in phase of "zero-crossing" markers on each cycle, as compared to the phase of the same markers during the control days, was plotted as a function of the time elapsed after the light-dark cycle phaseshift. An exponential function was fitted to the phaseshift of the rhythm phase markers. The circadian rhythms of activity, feeding, drinking, and body temperature phaseshifted significantly ($p < .05$) more rapidly than the urinary rhythms to the new light-dark cycle phase.

Previously, such internal desynchronization has only been demonstrated in human subjects isolated from all time cues by Aschoff and Wever and their colleagues (5) and more recently, also in man, in a collaborative study we have conducted with Elliott D. Weitzman and Charles Czeisler (8). However, there are some criticisms that can be made of data that can only be obtained from man, since with man's unique ability to control sleep-wake behavior volitionally it is possible, although unlikely, that artefactual internal desynchronization could be generated by an interaction between a single circadian oscillator within the subject and the volitional pattern of sleep-wake control. We have discussed this problem in more detail elsewhere (29). We therefore set out to examine whether we could identify spontaneous internal desynchronization of circadian rhythms within the squirrel monkey.

By placing the animals in a relatively bright light intensity of 600 lux of continuous light (LL) we were able to demonstrate in several animals clear instances of internal desynchronization between one or more rhythmic variables within the same monkey (29). An example of such internal desynchronization in the squirrel monkey is shown in Figure 7. The circadian rhythms of feeding and body temperature demonstrated a free-running period of approximately twenty-five hours whereas the circadian rhythms of urinary potassium and water excretion demonstrated a circadian period of twenty to twenty-one hours. Thus over the course of this experiment the temperature and feeding rhythms completed nine complete cycles whereas the urinary rhythms completed more than ten cycles, and internal phase angle shifts of more than 360° were thereby completed between these variables during the course of the experiment. Interestingly, a careful examination of the data shows that there was a partial phase locking between the two sets of rhythmic variables for the first four days of the experiment before the urinary variables totally uncoupled and demonstrated their spontaneous independent free-running period. This phenomenon has been termed by Czeisler "relative internal coordination."

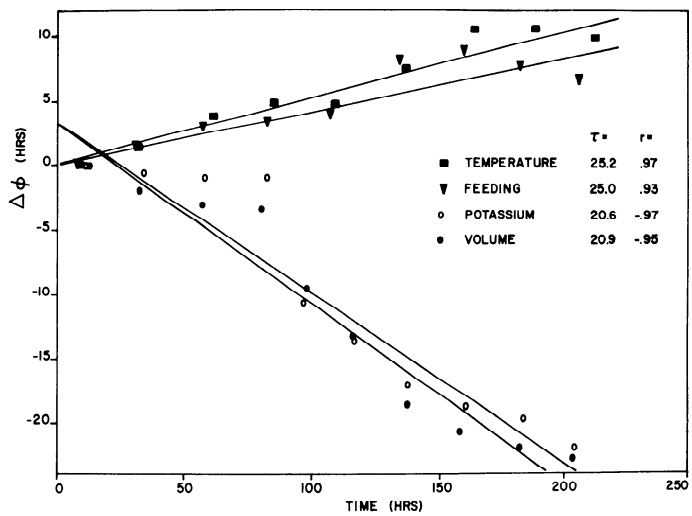

Fig. 7. Spontaneous internal desynchronization of the circadian rhythms of feeding and body temperature with respect to the rhythms of urinary potassium and water excretion in a squirrel monkey placed in constant light with no environmental time cues. The phaseshift of each variable as compared to the phase on the first day of LL is plotted against the elapsed time in days. The urinary rhythms complete an internal phase angle shift of more than 360° with respect to the other rhythms. These findings can only readily be explained by the existence of multiple circadian oscillators within the animal, and any single "clock" model is thereby made untenable.

This evidence clearly suggests that we are dealing with a multioscillator circadian timing system in the squirrel monkey. However, because with some ingenuity one can still devise ways in which a single oscillator within the animal could generate rhythms with different periods (most of these schemes are some variant of a slipping-clutch model) it is necessary to test some of the other predictions of the multioscillator system in order to confirm our conclusion.

One reasonable prediction of a multioscillator system is that it should be possible to remove tissues containing individual circadian oscillators from the animal and maintain them in tissue or organ culture *in vitro*. A number of experiments along these lines have now been conducted (we are reviewing them elsewhere) and there is evidence that rhythmic behavior will persist in isolated adrenal glands (1), liver cells in suspension (11), isolated heart (31), and erythrocytes (6). Although there are problems in the interpretation in some of these experiments, and there is sometimes a high degree of variability in the rhythmic patterns generated, there is now in our opinion a sufficient body of evidence of this nature to support the concept of a multioscillator circadian timing system with the various oscillators situated in various body tissues and even in every cell. Furthermore, extensive studies in many unicellular organisms demonstrate that single cells are capable of generating circadian rhythms (9,12). From this perspective also, a multioscillator timing system in higher animals seems the most probable organization.

The internal synchronization that is normally observed between circadian rhythms within the squirrel monkey suggests that there must be a mechanism of temporal communication among body tissues which transmits phase and period information between the various oscillators in the organism. Obvious candidates for temporal mediators in the circadian timing system of higher animals would be the circadian rhythms in plasma hormone concentration (4) and autonomic nervous system activity (7). In a single oscillator system all circadian rhythms in the organism would be forced responses originating from a single oscillator. In contrast a multiple oscillator system would demonstrate a different mode of temporal communication. Phase and period information would presumably be conveyed between the various potentially-independent oscillators by a mechanism of phase control analogous to the well documented mechanisms of phase control of circadian rhythms by light-dark cycles. To test this we have directed our attention towards possible internal mediators in the circadian system. As a result of this search, we have been able to demonstrate that the circadian rhythm in plasma cortisol concentration acts as an internal mediating cue which synchronizes the circadian rhythm of renal potassium excretion (22).

An examination of the mode of control of the renal potassium rhythm by the plasma cortisol rhythm demonstrated that plasma cortisol appears to exert phase control by the mechanism we predicted for a multioscillator system. The experiments used adrenalectomized chair-acclimatized squirrel monkeys with implanted venous catheters which led outside the isolation chamber so that cortisol could be infused into the animals without their being disturbed. Control of the phase, period and amplitude of the plasma cortisol rhythm could thereby be obtained without any handling of the animal. Figure 8 shows that when the phase of cortisol administration was phase delayed by eight hours the rhythm of renal potassium excretion resynchronized with respect to the cortisol rhythm over a period of three to four days. This gradual resynchronization suggested that the cortisol rhythm was not directly forcing the rhythm in renal potassium excretion. The rhythm of the animal's feeding in contrast remained synchronized to the light-dark cycle and thus was not shifted. That the final phase shift of the renal potassium rhythm was only 80% of the cortisol phase shift suggests that there exists some other pathway from the environmental zeitgebers which influences the phase of the

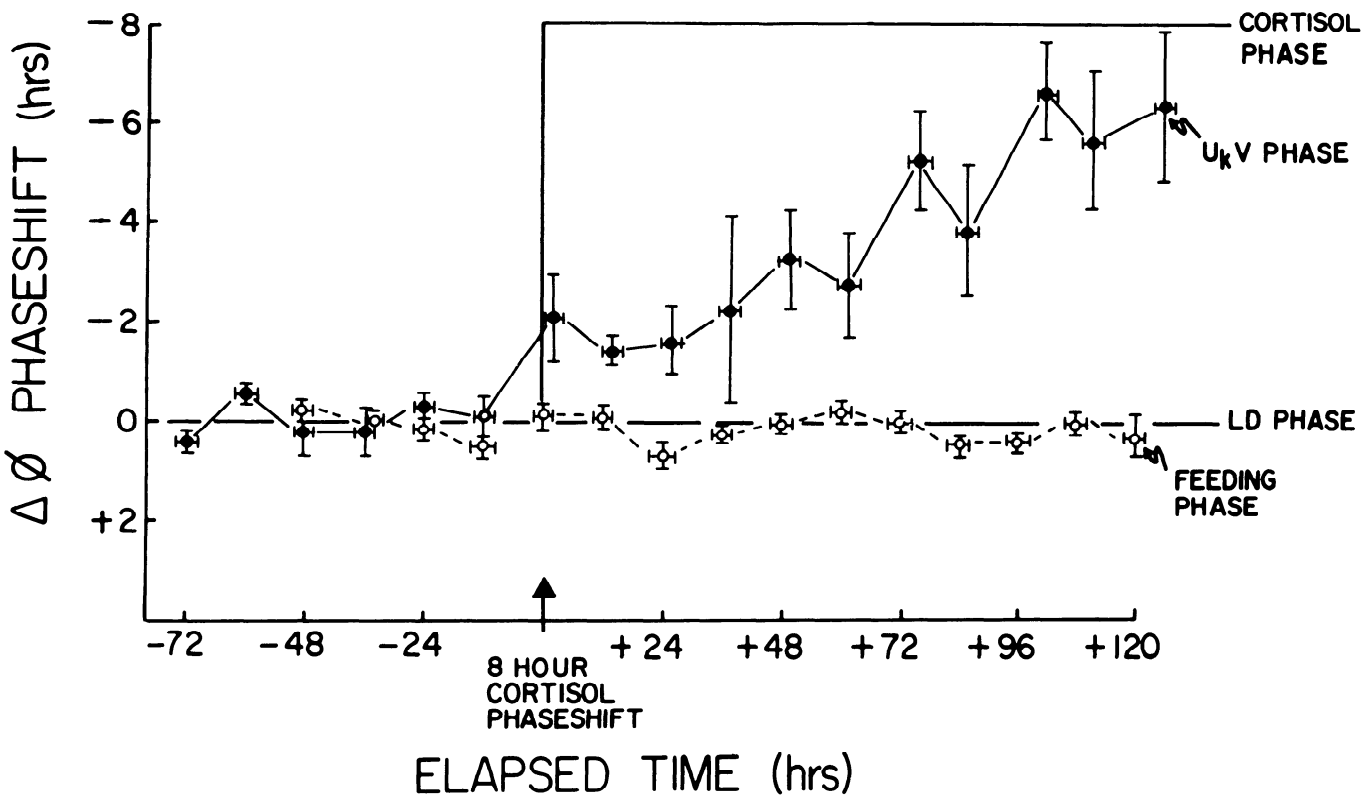

Fig. 8. Changes of phase (mean ± SEM) of the circadian rhythms of urinary potassium excretion (U_kV,●) and feeding (O) after an eight-hour phase-delay of the timing of cortisol administration in adrenalectomized monkeys. The phaseshift of each rhythm, as compared to the mean phase over the control period prior to the phaseshift, is plotted against the elapsed time in hours. The urinary potassium rhythm resynchornized with a phase delay 80% that of the cortisol phaseshift but the feeding rhythm remained synchronized to the light-dark cycle phase.

renal potassium rhythm, but it has approximately one-fifth of the coupling strength of the cortisol rhythm.

A key test of whether the renal potassium rhythm is generated by potentially-independent circadian oscillators is whether the renal rhythm will persist when plasma cortisol concentration is maintained without a rhythm. Accordingly, (Figure 9) we provided animals with a continuous intravenous infusion of adrenal steroids at the same twenty-four hour dose but evenly administered throughout day and night. When we did this the circadian rhythm broke up into a higher frequency oscillation in renal potassium excretion which was no longer synchronized to the light-dark cycle or other circadian rhythms within the animal. This again is strongly suggestive evidence that we are dealing with a multiple oscillator system where the internal coupling between the oscillators is maintained through hormonal and possibly neural mediators.

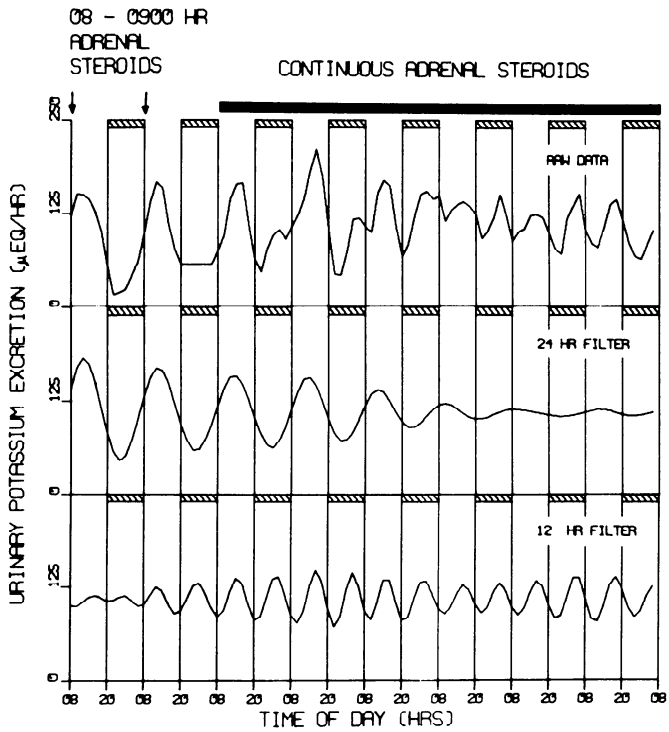

Fig. 9. Response to the continuous administration of adrenal steroids in an adrenalectomized monkey. For the first two days the daily dose of cortisol and aldosterone was administered between 08:00 hr and 09:00 hr. Then for the remainder of the experiment the same daily dose was evenly spread over each twenty-four hours. The top panel shows the raw data, the middle panel the output of a frequency filter centered at a twenty-four period and the lower panel the output of a filter centered at a twelve hour period. The circa-24 hour period damped out while an approximately 12.5 hour period gained strength during the continuous adrenal steroid administration.

We have discussed three corner-stones of evidence which strongly support the concept of the multioscillator circadian timing system in primates. The first is the demonstration of internal desynchronization between separate rhythmic variables within the system, the second is the demonstration that individual tissues can be maintained *in vitro* culture and continue to show rhythmic behavior, and the third is that the nature of communication within the system by hormonal mediators appears to represent the phase control of separate oscillators rather than the transmission of forced responses from a single driver. To this main triad of evidence we can add the observations of transient internal desynchronization between separate circadian rhythms within an animal after acute phase shifts of environmental zeitgebers and another reported phenomenon known as "splitting" in which different components transiently emerge out of the circadian rhythm of activity and appear to act independently (14).

Organization of the Multiple Oscillator System

The evidence discussed above indicates that we are now left to resolve whether the multioscillator circadian timing system is organized in a predominantly hierarchical (Model II) or a non-hierarchical (Model III) manner. As with the comparisons between single and multioscillator systems a number of possible tests between Models II and III exist.

The most obvious distinction between Model II and Model III is that Model II has a pacemaker while Model III has no one oscillator which consistently acts as a pacemaker. Therefore, if one could identify a pacemaker within the circadian timing system it would be possible to rule out Model III. A problem exists, however, if no pacemaker can be found since this could either mean that none existed (and it was indeed Model III that we were dealing with) or that the investigator had not been able to locate it within the circadian system.

The search for a circadian pacemaker in mammals has been pursued by a number of investigators. Richter placed electrolytic lesions at many sites in the brain as well as removing many endocrine glands (23). In the course of these studies he found that only lesions in the ventral hypothalamus significantly affected the circadian rhythms of rodents. Further studies by Zucker's group (25), Moore, et al. (17,18), and Stetson and Watson-Whitmyer (26) have demonstrated that the suprachiasmatic nuclei (SCN) of the hypothalamus appear to play a central role in circadian organization in rodents. These bilateral nuclei are situated on either side of the anterior tip of the third ventricle and receive the only direct neural input from the retina to the hypothalamus via the retino-hypothalamic tract (16). The early studies suggested that the SCN were the site of "the circadian clock." This evidence, which assumed a Model I type of organization, was based on the demonstration of apparent arrhythmicity in several normally-rhythmic variables after suprachiasmatic nuclei lesions.

This conclusion would be hard to reconcile with the extensive evidence we have discussed above which indicates that we are dealing with a multioscillator system, since a lesion at any one site should not cause arrhythmicity throughout the animal. However, more recent and extensive studies by Rusak (24) demonstrate behavior that is highly suggestive that the SCN may be playing the role of a pacemaker in a multioscillator system. Figure 10 shows the data from two hamsters which received total SCN lesions. The activity rhythms of each of these hamsters is double plotted to facilitate visual examination of the record. During the first few days of the experiment before the SCN lesion the hamster in each experiment demonstrated an activity rhythm which was synchronized with the light-dark cycle so that all activity occurred during the dark period of each day. Then after this baseline pattern was established SCN lesions were made in each animal at the time marked by the arrow. Subsequently, after each experiment was finished the totality of the SCN lesions was confirmed by histological examination.

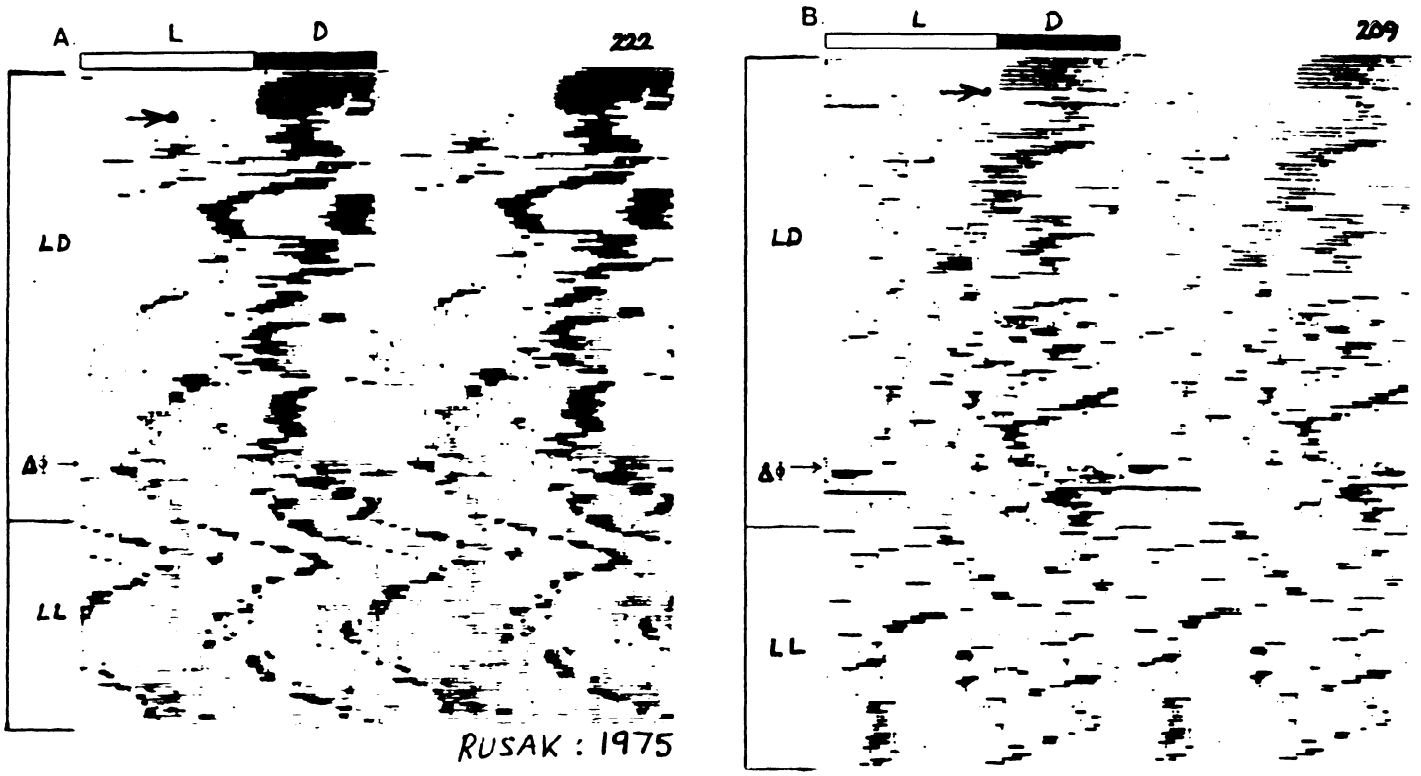

Fig. 10. Activity data from two hamsters in which SCN lesions were placed. The paper record of the animals' activity was cut into 24-hour segments and each segment placed under the previous day's. The data for each animal was then double plotted so that the first line shows Days 1 and 2, and the second line Days 2 and 3. After a few control days in LD, SCN lesions were placed at the time marked by the arrow. The animal was studied in the LD cycle, then after an LD phaseshift and finally in constant dim light (LL). The break up of the circadian rhythm into multiple wandering components can be readily visualized. [From Rusak (24)].

It can be seen from the record that the pattern of behavior was very far from being arrhythmic. Instead we see a break up into what appear to be multiple components running with different periods and showing much more instability than in the intact animal. In the light-dark cycle there was a tendency for the rhythms to demonstrate most of their activity during the time of darkness. However, when the animals were placed in constant dim light the different components of the activity rhythm can be seen to free-run quite independently of solar time.

These results are highly suggestive that the SCN act as a pacemaker in the circadian system. Functions, such as rest-activity cycles, would appear to be controlled by a pool of many oscillators which require the influence of the SCN for tight coupling. When the SCN are destroyed the internal coupling between these oscillators is insufficient to hold the rest-activity rhythm together and we see the wandering components. A major lesson from these observations of Rusak is that much more careful analysis of the data obtained from the suprachiasmatic lesioned animals must be undertaken. Particularly problematic are the conclusions of arrhythmicity that other authors (17,18) have based on experiments where groups of animals have been killed for each data point in the circadian cycle. This is the normal way to determine rhythms in pineal enzymes, for example, but the problem is that any single animal only contributes a fraction of the data for one phase of one circadian day. In these circumstances, since the different animals in the pooled data would each show their own unique and complex pattern, it would clearly be concluded that the effect of SCN lesions is circadian arrhythmia. From this sort of consideration we have to treat with caution reports of arrhythmia from pooled data on pineal enzymes, and plasma corticosteroid levels (17,18).

There are other ways in which we can examine whether we are dealing with a hierarchical (Model II) or a non-hierarchical (Model III) system. Because we know from our earlier discussion that cortisol is an internal mediator synchronizing the circadian rhythm of urinary potassium excretion, we have chosen to examine whether cortisol rhythms are capable through mutual interactions within the organism to synchronize other circadian rhythms (27). These experiments were conducted in our chair-acclimatized adrenalectomized monkeys in conditions of constant light so that the animal had no environmental time cues. A daily infusion of cortisol was administered to the animal through the venous catheter, thereby providing the only 24.0 hr cue. The results of this experiment (Table I) demonstrate that while the urinary potassium excretion rhythm was synchronized to a strictly 24.0 hr period, as would be predicted from our previous studies, the rhythms of feeding and body temperature free-ran with periods that were significantly different from twenty-four hours. This data supports the notion that the circadian timing system in the squirrel monkey is, at least in part, hierarchical in nature. In a non-hierarchical system one would have expected feedback interactions, through the pituitary-adrenal axis for example, to have a widespread effect on circadian timekeeping. Instead, the information appears to travel in one direction so only oscillators below the cortisol rhythm in the hierarchy are synchronized by it.

TABLE I

Periods of Circadian Rhythms of Squirrel Monkeys in LL Provided with Cortisol Daily at 08:00 hrs

Experiment Number	Urinary K+	Variable Temperature	Feeding	Days in LL
1	24.0**	24.5**	25.0**	8
2	24.0**	26.0**	25.0**	5
3	24.0**	25.0**	24.0**	9
4	24.0**	24.5**	24.5*	14

** = $p < 0.01$ * = $p < 0.05$

Another testable distinction between Models II and III is that in the most simple case a hierarchical model would have all conflicting time cues from the environment resolved at the level of the pacemaker. In contrast, our design of Model III would have any contrasting zeitgeber information being routed through different oscillators within the system. This difference in organization suggests that it should be possible to force rhythms apart from one another if we have a Model III type of organization.

We have now conducted an extensive series of tests of potential circadian zeitgebers in the squirrel monkey (28). We used the criteria that a circadian zeitgeber must a) exert period control so that the period of the rhythm of the animal (τ) must equal the period of the environmental zeitgeber (Υ); b) the zeitgeber must exert phase control so there is a reproducible phase angle (Ψ) between the animal's rhythms and the zeitgeber; and c) when the animal's rhythms are released into constant conditions after removal of the zeitgeber the initial phase of the free-running rhythm is determined by the previous phase of the zeitgeber.

With these criteria in mind we screened a wide variety of potential environmental time cues in the squirrel monkey with each time cue being tested individually in the absence of any other temporal information. Light-dark cycles (LD), temperature cycles (HC), social interaction-isolation cycles (SI), sound cycles (NQ), cycles of water availability (WT), and cycles of food availability (EF) were tested. Only light-dark cycles and food timing were found to be effective zeitgebers in the squirrel monkey (30).

A comparison of the effectiveness of light-dark cycles and feeding cycles in the synchronization of squirrel monkey circadian rhythms (manuscript in preparation) suggests that certain rhythms such as body temperature may be more tightly coupled to the light-dark cycle than to feeding cycles, whereas other rhythms such as those of urinary potassium excretion are more tightly coupled to feeding cycles than to light-dark cycles. This evidence suggests that there are different input routes to the circadian timing system and that all the temporal information is not solely resolved at a single pacemaker.

Because of this we have to propose some modification to our original models. While the evidence discussed above suggests that the circadian timing system has a predominantly hierarchical multioscillator organization it appears that not all environmental inputs are processed through a single input pathway. The most probable circadian organization in our view is some combination of Models II and III.

Now that we have the basic organizational plan of the circadian timekeeping system in the primate, the time has come to move from the abstract labelling of components as A,B,C, etc. to the specific identification of physiological components and pathways. Some progress has already been made in this, particularly with respect to the pathways involving the suprachiasmatic nucleus and in the pathways controlling pituitary-adrenal axis. A combination of techniques including the study of tissues *in vitro*, manipulation of putative neural and hormonal mediators and the detailed investigation of the location and mechanisms of putative oscillators within the system is required. A large amount of work needs to be done, but we feel at the present time we are well on the way to defining the anatomy and physiology of the system which measures circadian time in higher animals.

Summary

Extensive evidence demonstrates that the circadian timing system in primates is a multiple oscillator system which on occasion can become uncoupled. This system appears to be basically hierarchical in nature with the suprachiasmatic nucleus of the hypothalamus playing a role as a pacemaker in the system. This predominantly hierarchical organization is confirmed by studies which demonstrate that hormonal mediators appear to control only those rhythms below them in the hierarchy. However, studies of environmental zeitgebers in the squirrel monkey have demonstrated that the input of light-dark cycle phase and period information, and food timing phase and period information impinges on different points within the circadian timing system. Thus while the system may be predominantly hierarchical, the external inputs may enter at several levels.

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The evolution of the concepts discussed in this paper has in large part been a result of ongoing discussions with our collaborators. In particular we wish to acknowledge the contributions of C.A. Fuller, C.A. Czeisler, D.A. Kass, J.C. Zimmerman and L.G. Hiles. We are also most grateful for the assistance of M. McLaughlin, W.S. Schmelzer, and M.S. Harrigan. This work was supported by NASA grant NAS9-14249, NSF Grant PCM76-19943 and NIH Grant GN-22085.

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THE ROLE OF THE SOCRATIC TUTORIAL IN THE MEDICAL CURRICULUM*

Peter F. Hall
Department of Physiology
University of California
Irvine, California 92717

It has been pointed out elsewhere (1) that the future of Physiology is likely to be greatly influenced by economic pressures which may result in attempts to relegate this discipline to the Biological Sciences from which it came or to the Clinical Sciences which it came to serve. Because of its role at the interface between these two sciences and because Physiology is not a primary discipline like, for example, mathematics but is made up of contributions from a number of disciplines, there is more than one Physiology. The discipline reflects the special emphasis imparted to it by those who practice Physiology. Accordingly, the boundaries of Physiology are operational and to some extent flexible; flexible boundaries leave the discipline vulnerable to administrative manipulation. Biologists are likely to present Physiology in the broad context of Biology with little regard for its mission as the foundation of Pathophysiology. Clinicians, on the other hand, will present Physiology in fragments – the fragments needed as the foundations of each medical subspeciality. Physiologists must consider carefully whether either of these alternatives provides a satisfactory substitute for the Physiology which our Society has fostered during the last 80 years.

If the boundaries of Physiology are operational, we must examine the two principal operations involved in the practice of Physiology, namely, research and teaching. The consequences for research of dispersing the responsibilities of Physiology to other departments and schools form the basis of a different investigation but these consequences are likely to be far reaching. We are concerned here with teaching and the influence of the medical curriculum on the boundaries of Physiology and hence upon the extent to which it can be subject to administrative influences.

The traditional curriculum in Physiology for medical students consists of lectures and laboratory exercises. In recent years, laboratory exercises have lost favor, so that a course in Physiology for medical students sometimes consists of nothing more than a series of lectures. It might appear that such a program scarcely justifies the existence of a special department. It is relatively simple to organize a series of lectures with the aid of clinicians and biologists together with peripatetic lecturers whose number would increase in proportion to the demand.

There is, however, one important teaching device which is sometimes overlooked because it is frequently presented informally, namely the tutorial or small group discussion. The form and the significance of the tutorial are changing because it now serves some of the functions formerly expected of laboratory exercises. Such functions include student-teacher contact, informal discussion and the opportunity to consider the scientific basis of Physiology.

Importance of Tutorials. We might conveniently consider the pedagogic importance of the tutorial by attempting to answer two questions. Firstly, would a program in Physiology consisting only of lectures together with the laboratory experience necessary to complete a thesis, provide sufficient instruction for professional physiologists (i.e., graduate students)? Most graduate programs attempt to provide something more – something which challenges the student in order to promote intellectual independence. This additional element is hard to define but is no less important for that. It has to do with assuring the student and those responsible for his instruction that he can use experimental data to construct useful conclusions which are consistent with available evidence. That is what Physiologists themselves do and what they train their professional offspring to do. An expression sometimes used to describe this form of instruction is problem-solving. Some such form of discussion between teachers and students would appear to constitute an essential ingredient in a graduate program.

Secondly, does the physician serve as a professional Physiologist at the bed-side? Contemporary medicine approaches disease through pathophysiology. In the case of diseases in which there is no sharp distinction between normal and abnormal, there is no alternative. How can one approach hypertension except through the normal regulation of blood pressure? The pages of such publications as the Journal of Clinical Investigation abound in Physiology – human physiology but physiology none the less. The physicians who contribute to these pages and those who read them must surely be Physiologists. This point of view becomes clearer with the aid of an example. At present, the physiological significance and the therapeutic potential of the substance somatostatin are uncertain; physiologists and clinical scientists are investigating this fascinating substance (2). The physician might wait until these investigations reveal some clinical use for the hormone; he could then use somatostatin under instructions with little understanding of what somatostatin is and where it comes from. If we regard such practice as satisfactory, it follows that we are training our physicians incorrectly since we are at great pains to make them understand, for example, how insulin acts and where it comes from. If we are to offer physicians the opportunity of understanding how somatostatin acts, they must be able to follow the growing insight into the physiology of this substance long before it becomes a therapeutic agent (if indeed it ever does). In this way, somatostatin can be presented as something we have come to understand instead of being produced like a rabbit from a hat. The idea that the future physician should be spared the necessity of understanding how we know the facts of Physiology (as though this were a punishment), but should learn lists of documented conclusions, is simply not worth discussing. The view that there is one kind of Physiology for the physician and another for the physiologist can only reflect a fundamental misunderstanding of science in general and medical science in particular or a rationalization of the need to regulate the cost of training the physician. To be safe and effective the practice of medicine must be based on something more than blind empiricism – it must be based upon pathophysiology and the physician must be trained in the first instance as a physiologist.

*Presented at the Fall Meeting of the Association of Chairmen of Departments of Physiology in November 1976.

None of this is new and the traditional use of laboratory exercises served to bring the future clinician close to the inner workings of Physiology. Unfortunately, a variety of problems have made the laboratory exercise less readily implemented than before. If we can use the tutorial to discuss the experimental evidence that medical students cannot obtain for themselves in the laboratory, we can continue to train physicians as physiologists and we can avoid the problems associated with laboratory exercises for medical students. Such a curriculum will require of the teachers an intellectual breadth and a commitment not readily achieved by exponents of other disciplines for whom this form of instruction will be at best a second interest. Before we consider how these things can be accomplished, it will be useful to examine the present state of the tutorial in medical curricula throughout the country. For this purpose, two definitions are important. A tutorial or small group discussion is defined as a discussion directed by a tutor with the participation of a small number of students (usually less than twenty). 'Socratic' describes tutorials based upon questions posed to promote discussions which in turn may solve problems, result in guided discovery or reveal problems not otherwise considered. It is assumed that tutorials, whether socratic or not, will result in considerations that arise from contributions from the group such that the result is more than the sum of the individual contributions.

The Questionnaire. Information obtained by questionnaire from Chairmen of Departments of Physiology in this country is summarized in Tables I-III and in Figure 1. It will be seen that more than 80% of responding schools use tutorials (Table 1). These tutorials commonly last two hours, occur 10-20 times in the curriculum with groups of less than 20 students. In most cases (88%) the format is socratic; it may be organized or left up to individual tutors and in most cases (78%) each tutor discusses material outside the area of his expertise (Table III). Most Chairmen believe that tutorials are very useful, fewer feel they are of some use and one gave the opinion that they are of no use (Figure 1). Sixty-six percent of responding Chairmen said that experimental evidence was used in the tutorials.

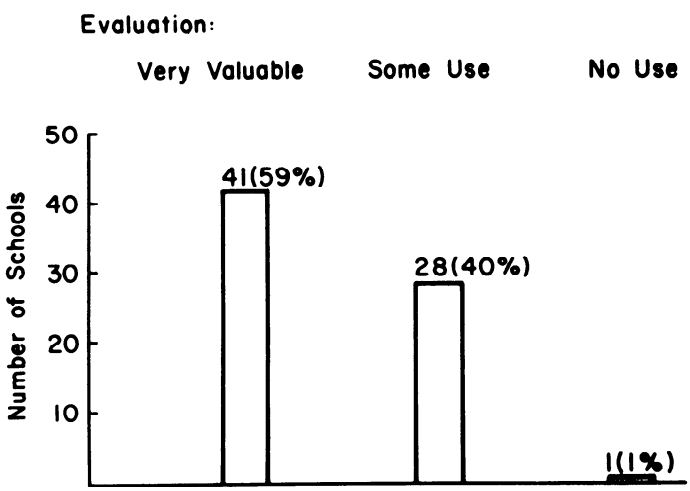

Fig. 1. Chairmen of departments of Physiology in the U.S.A. and Canada were asked to give their opinions concerning the merits of tutorials. They were asked to choose between the three possibilities shown. The total number of responses was 70.

TABLE I

Medical Curriculum: Tutorials in Physiology

Schools using tutorials:	80	(81%)			
Total Number/Course:	<5	5-10	11-20	>20	
Number of schools:	5	15	42	14	
Length (hours):	1	2	>2		
Number of schools:	18	56	5		
Number of students:	<5	5-10	11-15	15-20	>20
Number of schools:	1	22	26	15	11

The total number of accredited medical schools in America was 114 at the time of the investigation. Not all responding chairmen answered all questions shown in this and the following tables.

TABLE II

Format of Tutorials in Physiology

Socratic:	64	(88%)		
Content:	Review of Lecture Material	Experimental Evidence	One topic per session	
No. of schools:	56	53	44	

Values are based upon the number of complete answers. Clearly, some schools used more than one approach to content.

TABLE III

Organization of Tutorials in Physiology

Organization:	Open	Planned	Handouts
Number of schools:	26	29	17
One tutor – All topics:	64 (78%)		
Acceptance:	Well Accepted	Indifferent	Opposed
Number of schools:	20	6	6

Some caution is necessary in interpreting the results of such a questionnaire. For example, a Chairman can only attend his own tutorials and cannot easily speak for other tutors. Nevertheless, it is clear that tutorials are widely used and that in many cases faculty teach all the major aspects of Physiology – this is a responsibility that clinicians and biologists might hesitate to assume.

The tutorial can make two important contributions to Physiology: 1) it provides the important element of problem-solving within the context of scientific method, and 2) it increases contact between professor and student. These contributions emphasize the special role of the Department

of Physiology in medical education. We must, therefore, consider the format of the tutorial in the light of these functions.

Format of Tutorials. In general, there are three main types of tutorial in current use, although some mixture of the three prototypes may well be the most common: Type I, small group review of lecture material – this may be formal or informal; Type II, specialist review in which each professor reviews his lecture material for the class in small groups and Type III, socratic tutorial in which experimental evidence provides the basis for discussions which go beyond the lecture material. The desirable elements in a tutorial serving the functions described above might be summarized as follows: (a) socratic discussion; (b) new material, i.e. material not presented in lecture; (c) experimental evidence; (d) stable student-tutor groups and (e) assigned times and topics. (a-c) provide intellectual challenge, (d) enables important group dynamics to emerge and (e) encourages some uniformity between different groups, facilitates scheduling in crowded curricula and provides visibility to the administration. The last point deserves emphasis because the tutorials have been overlooked as an important element in teaching programs when they are given in unscheduled time.

Undesirable elements would include the following: (a) mini-lectures, (b) questions answered always by the same small number of students, (c) gross lack of uniformity between groups, and (d) tutorials devoted only to review of lecture material.

By avoiding (a) the students must participate in discussions. If (b) and (c) are avoided, all medical students can share the advantages of tutorials and avoiding (d) insures that tutorials provide new ideas for discussion so that repetition of lectures is avoided and the tutorial becomes an independent vehicle for instruction. When these features of the tutorial are considered in relation to the three prototypes, the following profiles emerge:

Features of Tutorial	I Review of Lecture Material	II Specialist Review	III Socratic Tutorial
(a) Socratic Discussion	–	–	+
(b) New material	–	–	+
(c) Experimental Evidence	–	–	+
(d) Stable Group Composition	+	–	+
(e) Assigned Time	+	+	+
(a) Mini-lectures	±	+	–
(b) Few participating students	±	±	–
(c) Non-uniformity between groups	+	+	–
(d) Review only	±	–	–

Clearly the socratic tutorial can provide all the elements needed to allow the tutorial to serve the functions described above and can avoid features which work against these functions.

Implementation. Successful implementation of any system of tutorials requires cooperation between faculty and students. In addition, present administration of medical schools requires that any departure from traditional methods receive the sympathetic support of our Deans.

1. Faculty. The proposed format of tutorials requires a considerable contribution by the faculty who must understand the purposes of the tutorials. The faculty need to attend lectures, at least initially and some type of faculty interaction is necessary to facilitate uniform presentation of material not part of their special interest within Physiology. They must also understand the fundamental features of socratic discussion. However, if tutorials are well prepared and few changes made from year to year, the faculty will not find the task beyond them. They should also see that tutorials are less time-consuming than full-scale laboratory exercises.
2. Students. The pressures under which students enter medical school today generate attitudes and ideas which are incompatible with good performance in socratic tutorials or, for that matter, with full acceptance of the scientific basis of medicine. It is necessary to see that students understand that Physiology consists largely of experiments and that to avoid the experiments is to avoid Physiology. They must understand that socratic questions are vehicles for discussion – in many cases there may be no satisfactory answers to such questions. To this end, the inevitable effects of multiple-choice examination questions must be eradicated – that is the idea that Physiology is a series of black and white questions to which there is in each case a single correct answer must be replaced by a more mature and realistic understanding of the scientific method. This is especially important when the curriculum contains no laboratory exercises. Without any laboratory experience and with the threatening shadow of National Board multiple choice questions, students could come to learn Physiology only through the review books available for cramming. In addition to clear statements to the students of these considerations, it is necessary to devote a significant part of examinations to the material presented in tutorials. Contemporary college education (especially pre-medical education) is based upon inordinate emphasis on examinations and grades which have become ends in themselves.
3. The Dean. Our Deans have found it necessary to interfere with the academic process in a variety of ways so that any significant change in the curriculum needs the Dean's support. It is important that the dean appreciates the objectives of the small group discussion and the extensive investment of faculty time which successful implementation of tutorials requires. He should also be made to understand the economic gain of using the tutorial in partial substitution for laboratory exercises. Finally, the Dean should also understand the academic and political consequences of alternative arrangements for the teaching of Physiology.

An example of the type of material presented at the University of California, Irvine, will illustrate some of these points. In the cardiovascular lectures, students are given a conventional account of the distribution of muscle, elastic tissue and collagen in the various parts of the vascular tree.

Some hours before the relevant tutorial, they are given a figure from the studies of Burton et al, Figure 2, (3) with a legend describing the experiment in which tension is plotted as a function of initial length for the intact vessel, for the vessel treated with trypsin to remove elastic tissue and for the vessel treated with formic acid to remove collagen. The students are asked to interpret the data and without being told, they reach two important conclusions: firstly, that on stretching, the intact vessel behaves like a mixture of elastin and collagen and secondly, at the resting length collagen is unstretched because the collagen component of the curve for the intact vessel is not seen until the vessel is stretched beyond that length (Figure 2). The second point requires considerable "socratic probing" but eventually with continued questioning about the state of collagen in the unstretched vessel and the relationships between the three curves the point is "discovered" by the students. The tutor points out that in the unstretched vessel collagen is found in the slack loops. This is followed by a figure from the same paper (not shown here) in which similar curves are given for arteries from subjects of various ages (3). Here the students "discover" that in arteries from older subjects some collagen is stretched at or close to the resting length and 50 percent of the fibers are stretched at a shorter length than with arteries from young subjects. This provides a vehicle for a discussion which reveals the importance of physiology in understanding processes such as arteriosclerosis and ageing.

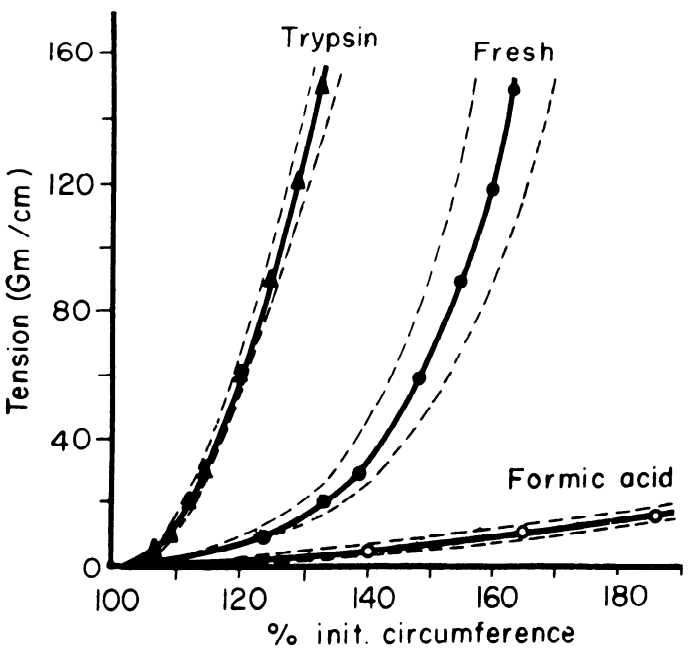

Fig. 2. Length-tension diatrams for human arteries. The figure shows tension as a function of length for intact arteries, arteries treated with trypsin and arteries treated with fomic acid. Reproduced with permission of the authors from the Canadian Journal of Biochemistry and Physiology. (Note: this legend is not provided for the students).

It is believed that a well-conducted discussion along these lines causes the students to consider the relationship between structure and function in the vessel wall very closely, and that the element of discovery leading to clarification brings them close to the scientific method and provides the sense of satisfaction so essential for good motivation. This is the element of intellectual challenge or problem-solving.

In contrast, a formal statement of the results of this study in lecture provides another two facts for the students to learn; by not participating he loses the advantage of discovering for himself. On the other hand, a laboratory exercise to repeat these studies would be time-consuming and difficult to execute. Most students would produce unsatisfactory data and in any case, there would be no process of discovery, because it is difficult to organize such a laboratory exercise without the students knowing the expected result. In addition, the experiment in tutorial can be used to review the background material presented in lecture. The tutorial can provide the opportunity for review of other material not directly related to the experiments presented.

In spite of the importance of protecting Physiology from meddlesome interference, there is probably little enthusiasm for curricular changes based only on political expedience. However, if heuristic and political considerations point in the same direction, enthusiasm is likely to be that much greater. One might wonder if these ideas merely lead to short-term perpetuation of something that was created by a need that no longer exists. It might be thought that perhaps Physiology has run its course and is ready to return to Biology or that large departments of medicine can provide all the Physiology that medical science requires. These are times of sweeping change and no one can see what the future holds. If administrators who do not appreciate the history of Physiology and its contributions to Medicine are allowed to make radical changes without bearing the responsibility for problems these changes may produce, Physiology could suffer a serious setback. When the future of medical education becomes clear and Physiology is seen as an essential component of such education, it may take much time and effort to restore the discipline to its present state.

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ABSORPTION AND OSMOSIS: FRENCH PHYSIOLOGY AND PHYSICS IN THE EARLY NINETEENTH CENTURY*

J.V. PICKSTONE
Senior Research Fellow,
Department of History of Science and Technology
UMIST, Manchester

In 1826, Henri Dutrochet, working in his small chateau near Chateau Renault in the Touraine, put a snail sperm sac into water in order to examine it under his microscope. He noticed that the contents were extruded from the open tip of the horn, as if pushed out by a piston. The movement was easily visible for the dense contents contrasted with the water outside. The movement stopped when all the dense fluid had left the capsule (1).

Dutrochet was reminded of an observation he had made 16 years earlier, about the time he had been invalided out of the French army medical corps and had settled at his mother's house and begun research into the anatomy and physiology of plants and animals. He had then examined the capsules of a fungus growing on a fish and had seen the contents expelled. He had reported the observation to the Société Philomatique in Paris, but had not pursued the study, thinking that he might have been the victim of an illusion due to the microscope. But now, in 1826, his wide ranging microscopical studies on lower animals and plants had led him to make a similar observation, this time on a larger object. For reasons I shall discuss, he attempted a causal analysis of the expulsion of sperm and adopted the hypothesis that the dense fluids within the capsule were responsible for the inflow of water which forced the contents outwards.

He then made a model of the system. Having made a sac from a portion of chicken gut, he filled it with milk, closed the end, and immersed the sac in water. As expected it swelled.

From this model Dutrochet went on to devise the endosmometer, still familiar in biological laboratories, at least in schools. A gut membrane was tied over the end of a piece of glass tubing. When dense fluid was placed inside the tube and the apparatus immersed in water, the level of liquid inside rose. By the end of October 1826, Dutrochet was ready to report his findings to the French Academy of Sciences, of which he was a corresponding member. By this time he had shown that the inward movement of fluid was accompanied by the outward movement of some of the dense fluid. He had also shown that the movement was not always of dense fluid to less dense; when alcohol or certain acids were tested, against water, the reverse was true; results which led Dutrochet to suppose that the fluid movement might result from electrical differences across the membrane, produced, on the analogy of the voltaic pile, by differences of density or of acidity.

At this stage Dutrochet thought that the phenomena were restricted to organic membranes. He referred to endosmosis as a phenomenon of organic physics. But it was more besides. Dutrochet had long been convinced that life was fundamentally motion. Now he thought he had discovered the immediate agent of that vital motion: here was the secret of vegetative life and perhaps of animal life too. His book which set out these claims was well under way when he came to Paris to announce his findings.

He did not wait long for criticism. At the end of the paper, François Magendie rose to begin the debate (2). He was slightly younger than Dutrochet, but had been educated at about the same time in the Medical School of Paris. Magendie had remained in Paris, and had rapidly established a reputation as a physiologist. By 1826 he was the editor of the first French journal to be devoted largely to experimental physiology, and he was already a full member of the Academy, within which he maintained a proprietorial attitude towards physiological matters. He was also an authority on the physiology of absorption, and far from convinced that Dutrochet had discovered anything new.

Had not Magendie himself shown in 1820 that physiological absorption could be understood as imbibition, due to capillary action in the pores of membranes (3)? The young Sicilian physician, Michel Foderà, had extended Magendie's work to show that materials could move across living and dead membranes in both directions at once. And he had shown, following the Englishman Robert Porrett, that an electrical current flowing across a membrane could result in a rapid movement of fluid (4).

There followed a debate as to whether or not Dutrochet's results could be explained by capillary action. Magendie's suggestion to this effect was elaborated by the mathematician S.D. Poisson. The electrician André-Marie Ampère supported Dutrochet in resisting this notion. Laplace himself took part in the discussion.

Here, in this debate at the Academy, we find epitomised the problem with which this paper will attempt to deal. I hope to show, by considering the relevant work of Magendie, of Foderà and of Dutrochet, what was at issue among them and where the roots of misunderstanding lay. I shall argue that we have here, not just a particular difference over physiological explanation, but a confrontation of three approaches to the physiology of tissues. During the 1820s, at least two of these approaches were appearing for the first time, but their confrontation was to be characterisitc of much physiological thought later in the century.

By analysing this historical situation I hope to show how certain key biological ideas entered the area of experimental physiology, and how an experimental physiology of tissues and a general physiology of cells took shape in early nineteenth century France. In doing so, I hope to contribute to a more general project: that of mapping the patterns of thought and research in the development of physiology. We still know little more than a few peaks on this map, and even for these few areas that have been studied, we cannot as yet see very far into the connections between the physiology and the societies which produced it.

Perhaps this paper may help a little towards the elucidation of one such historical problem already raised in the literature: the relative decline of French physiology by the mid-century. It has been suggested that French physiology was predominantly organismic and therefore was mined out, at about the same time as the Germans began to exploit a more biophysical style. I shall not deal here with the organ physiology, but we shall see enough of tissue physiology and the application of

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physical sciences to demonstrate the wide range of approaches current in France. The problem of national differences must become one of selective processes acting differently on a similar range of approaches (5).

When a full assessment is made of these various selective processes, the period of the 1820's will probably appear as critical. Conspicuously, at the beginning of the decade, physiology was very much the subject of the day. It was generally recognised that what we might call the edge of objectivity had passed from chemistry onto physiology; physiological investigations occupied some of the brightest young investigators in Paris, and were actively supported by many prestigious Academicians. By the end of the decade, the best of these workers were engaged on other subjects. Almost certainly the failure to provide employment opportunities contributed to that loss of impetus, but we will also have to consider how successful the physiological ventures were, compared with contemporary work in such established fields as organic chemistry and anatomy.

Before we can even begin to study such mechanisms of selection, we need to analyse the strands of physiology. This paper is devoted to comparing the formulations by Magendie, Foderà and Dutrochet of the problem of absorption.

THE WORK OF FRANÇOIS MAGENDIE ON ABSORPTION

Magendie published his first study on absorption in 1809, at the start of his career as a physiologist (6). From that time on, certainly up to 1826, he was the major figure in the field, stimulating argument and experimental studies.

The centre of his work was the claim that the veins rather than the lymphatic vessels were responsible for absorption, other than that of chyle from the gut. This might reasonably be understood as a research programme in opposition to the view dominant during the last quarter of the 18th century, that the lymphatics, and they alone, were the absorbent system.

The experiments which the young Magendie performed in 1809 on the mode of action of strychnine poisons, afforded him an opportunity to question severely the doctrine of lymphatic absorption. Since Magendie does not appear to have taken seriously the possibility that the poisons acted directly through nerves, without absorption, the rapidity of action must have immediately led him to doubt the role of the lymphatics. A series of experiments using gut sections and limbs, isolated except for connecting blood vessels, convinced him that the poisons, injected into the gut, or placed in tissue wounds, were taken up by veins, and thus transmitted to the site of action, the spinal cord.

Without going into the debate over these experiments, I would emphasise two features of Magendie's work:

i) like his antagonists he was concerned with vessels.

ii) like them he thought largely in terms of one system/one function. Magendie gained a reputation for polemic, not for asserting that some substances, notably poisons, may be absorbed by veins; but for trying to replace lymphatics by the veins as the set of absorbent vessels.

But this was not just a swap of one set of vessels for another. Though Magendie tried to claim that veins were the absorbent vessels, he did not deny that chyle was absorbed through the lacteals. Nor could he maintain that absorption was the only function of the veins. Thus, in two respects, his innovations damaged the one system/one function equivalence which had attracted eighteenth century physiologists to the

Fig. 1. François Magendie, a portrait by Paul Guérin, reproduced from Les médecins célèbres, Editions d'art Lucien Mazenod, Genève, 1947.

doctrine of lymphatic absorption. Further, to move from the lymphatics to the veins was to abandon a set of vessels thought to have active, open mouths, for a system of vessels which, in as much as they were accepted as continuous with arteries, could have neither open mouths nor rootlets. Not surprisingly, Magendie initially dismissed the problem of uptake and concentrated on the establishing of the routes along which absorbed materials passed. By doing so, he demonstrated again that in his work, functions had begun to take priority over organ systems. He tried to find out how the function of absorption was performed, rather than concentrating on the operations of a particular set of vessels.

In 1820 Magendie attempted to explain uptake, proposing that absorption took place by imbibition through the walls of vessels, by the physical process of capillarity. The arguments for and against this idea had been aired frequently, though usually in the context of exhalation or transudation, the twin problem to that of absorption. Magendie's evidence was interesting but far from conclusive. The appeal of the position derived from more general considerations.

Firstly, it complemented the claims for venous absorption, since if accepted, it disposed of the problem of absorbent mouths. Secondly, it transferred to simple pores and physical forces the properties which the older physiology assigned to special open rootlets and their sensibility. Of course the identification of absorption with imbibition was crass. There was some selectivity in absorption and the problem of maintaining the separateness of fluids did require a solution. Magendie did his best to brush the problems aside, asserting that the structure of membranes was such that they must imbibe, in life as in death.

I would suggest that Magendie in 1820 had a dual concern: to support the case for veins, and to assert the relevance of physical science to physiology. Unable to articulate the problem of how physics and physiology might be related, he contented himself with picking out certain pieces of physics which bore some obvious analogy to physiological phenomena,

and so strengthened his assertion that the stuff of animal bodies was essentially the same as the stuff of the inorganic world.

It is useful here to look at Magendie in the context of science in Paris. He aspired to enter an Academy dominated by anatomists and by prestigious physicists and chemists. His own chief claims to fame were his researches in anatomical physiology, such as his studies of the routes of poison. But what was he to say about the physiology of tissues, having rejected the kind of anatomical extrapolation which had served Bichat?

The organic chemists were busy exploring the composition of various kinds of animal matter and Magendie could begin his physiology textbook with an account of the chemistry of the body constituents. Electricity looked promising as a means of explaining such phenomena as secretion. Generally, physical sciences seemed to be unravelling the problems of animal physiology, refuting the assertions of the medical vitalists, and confirming the position long held by certain disciples of Lavoisier, that physiology was really a branch of physics. The particular example of Laplace may have been an important influence on Magendie. We know that Laplace assisted the young physiologist (7), we also know that Laplace was the major contemporary authority of the physics of capillarity.

Thus when Magendie in 1820 adopted the capillarity hypothesis, he was not only aligning himself with the general theoretical position of an important group of Academy physicists, he was adopting a specific mechanism which they had sought to elucidate for inorganic bodies. In 1826, as we have seen, when Magendie claimed to explain osmosis in terms of capillarity, he was supported by the mathematician Poisson, whose short note on the topic was later published in Magendie's journal.

I would suggest then that Magendie's physiology had a double structure, not unrelated to the distribution of interests within the French Academy. On the one hand his mammalian physiology linked up with the comparative anatomy of the Cuvier school; on the other hand he sought to use contemporary physical science. In the words of an anonymous but contemporary reviewer, he sought to translate the science of inorganic bodies into physiology (8). It was for him, in part, a matter of prestige that medical men should learn some chemistry and physics.

FODERÀ AND THE PROBLEM OF TISSUE ABSORPTION

In several ways, the attitude of Magendie towards the problem of absorption recalls the mechanical vascular physiology of the 17th and early 18th centuries; the same stress on vessels, linked with a mechanistic hypothesis concerning the permeability of the vessel walls.

Yet, closely associated with Magendie's researches, we find the beginning of a new problem, that of tissue absorption. It is a problem posed within a biological perspective, one which involved reference to the common functions of all animal tissues. I shall suggest that we see the first clear formulation of the new problem in the work of Michel Foderà, a Sicilian philosopher, physician and physiologist, who, though closely connected with Magendie's experimental studies about 1820, was more open than his master to the innovations of French general anatomy and French zoology, and who, especially, was connected with the zoologist Henri Blainville, chief source of the biological theories expounded in 1830 by August Comte (9). It was Comte who popularised the notion of biology as a unified science of life, who stressed that life was a process of interaction between organism and environment, and who insisted on the peculiar features of living bodies at the same time as he asserted the relevance of general laws to the behaviour of all kinds of matter. Thus, I hope here to elucidate one connection between Positivism as a philosophy of biology, and the progress in the laboratory study of absorption.

First the nature of the problem shift. In the physiology of the mid-19th century, as in more recent physiology, the role of the lymphatics and veins in moving absorbed fluid had been made secondary to the problem of tissue absorption, or later, absorption by cells. The experiments and arguments about veins and lymphatics which had constituted almost the whole topic of absorption in the early 19th century, became subsidiary matters of transport; the primary phenomenon was the uptake of fluid by the non-vascular tissue stuff.

This problem structure was well exemplified, for example, in an article on absorption written in 1864 by Paul Bert, pupil of Claude Bernard (10), but we can find the same formulation in a review written in 1829 (11), as a result of which a late edition of Richerand's well-known physiology text referred to three revolutions in the study of absorption: that instituted by the Hunters' work on the lymphatics, the work of Magendie on venous absorption, and thirdly the more recent shift which made the veins-lymphatic dispute peripheral, in posing the problem of tissue absorption (12).

Who then was seen as responsible for this shift? The answer is that no one person was wholly responsible, nor did anyone push the issue, as Magendie had pushed venous absorption. But if we look for the earliest clear formulation, or to the source of the evidence on which authors drew to discuss the shift, then the results, in both cases, at least as far as France is concerned, point to Michel Foderà's prize winning studies on the movements of various easily recognised chemicals through the tissues of the body. The work was first reported in 1822. Foderà had used a number of substances, but chiefly potassium prussiate [ferrocyanide] to demonstrate movement across the walls of tissue sacs, in vitro, and within the animal body. He had shown that substances could pass in two directions simultaneously.

In some respects Foderà's work was a direct outgrowth of Magendie's. The imbibition hypothesis complemented the doctrine of venous absorption, as long as the case was argued against proponents of lymphatic mouths, but, if the physical hypothesis was taken seriously, it began to undermine the whole anatomical problem. If veins absorbed because their walls were made of animal matter which was naturally porous, then lymphatics ought to absorb for the same reason. By 1826, Magendie, had realised this, when he wrote in the second edition of his textbook:

> I have proved by a series of experiments that all living tissues imbibe all liquid materials which touch them; the same effect is produced with solids, provided that they be soluble in our fluids and particularly in blood serum.
>
> This general fact being established, the absorption which has so much occupied the physiologists, which has so exercised their imagination, produced so many disputes, becomes a phenomenon of the simplest kind, almost entirely physical. One no longer will discuss whether it is the veins or the lymphatics which absorb, since all the tissues are endowed with this property (13).

But his slowness in recognising this development, his continuing attention to the venous-lymphatic dispute, and his failure to draw much attention to the studies on tissue absorption, lead me to suppose that Magendie would not, alone, have come to write the passage I just quoted. Certainly Foderà expressed this attitude earlier, and in a much richer way.

Perhaps Foderà's knowledge of Italian physiology was a minor help here; his loyalty to the conclusion of Paolo Mascagni, the great Italian student of the lymphatics, predisposed him to welcome a compromise on the vein-lymphatic issue (14). But Mascagni gave him more. Mascagni had studied the microscopical structure of intestinal villi, and, like several later German anatomists, especially C.A. Rudolphi, he had failed to find the open mouths so dear to the lymphatic doctrine and so graphically described by several British anatomists. Rudolphi had argued that the villi acted like sponges, to soak up fluid, which only then passed into veins or lymphatics (15).

Microscopes had been little used in France before about 1820. The suspicion which surrounded them was fed by disputes over the shape and size of blood corpuscles, or the fine structure of the tissues, and it found expression in Bichat's well quoted remark that to look into a microscope was to look into the dark, each man would see what he wished to see. But in the early twenties there was a revival of microscopical studies. Several of the younger physiologists in Paris were beginning to study the structure of body parts. Foderà certainly made a number of studies. Indeed he promised to write a book on the tissues of lower animals, a good idea which did not materialise. He did, however, confirm that the intestinal villi did not have obvious openings. Fluid must first be taken up into the cellular tissue which covered the villus.

This notion of indirect absorption was current in France around 1820, but as long as one thought of tissues simply as a barrier to be crossed by material entering vessels, the notion was of little significance. But we have yet to examine a dimension of physiological thought very characteristic of certain French groups, especially the group round Blainville, namely, the animal series. In this perspective, the passage of materials into non-vascular cellular tissue could become important, for such tissue appeared to be the basis of the simplest animals.

Since at least the time of Vicq d'Azyr, a comparative dimension had appeared, more or less, in all French physiological writing. In connection with absorption, the lower animals (a lower animal from 1750 to 1830 was usually a polyp) were seen as taking food materials into their substance, directly from the surrounding medium. It was customary among French vitalists to speak of this "movement of nutrition" in the simplest forms; but almost all writers, when they came to discuss the higher animals, and thereby introduced vessels, saw them, not as aids to this nutrition in the tissues, but as themselves the primary focus. The centre of a higher animal according to Bichat and his followers was the blood; various kinds of absorption, from gut, from lungs, or from the tissues themselves, served to introduce different kinds of fluid into the blood. The passage of this blood into the tissue spaces was a matter of transudation or exhalation through exhalent arteries. The focus was the blood, the mechanisms were all referred to vessels (16).

We see then, in the hey-day of general anatomy in France, when the notion of tissue was being hailed as a major gain for medical science, that the nub of tissue physiology remained vascular as far as the higher animals were concerned. The physiology of tissues was constructed by analogy with previous vascular physiology.

The shift instituted by the biologists, Blainville and his associates, put tissues, non-vascular tissues, first. They did so because, in their attempts to found a unified science of life which they called biology, they drew on Lamarck (and perhaps on the German school) who had not only introduced that term in France, but had done so in connection with studies of lower animals. For Lamarck, it was the lowest animals which most clearly demonstrated the basic properties of life. For Blainville, whether one analysed the tissues of higher animals, or looked back at their embryos, or looked down to the lowest animals, one was led to cellular tissue, a non-vascular, fibre matrix which provided his basic picture of living material. It was to this tissue that a physiologist must address himself. In higher animals one might find auxiliary mechanisms, but one would still find the fundamental phenomena common to all life (17).

The principle of reasoning was well set out by a student of Blainville:

> It is an incontestable principle that what is observed in the lowest animals, in which animality is, so to speak, reduced to its most simple expression, must recur in the higher animals (18).

Its application to the physiology of absorption was made crystal clear by Foderà:

> A theory of these functions must, to be perfect, accord with all phenomena of life, and emanate directly from general physiology. In fact, how can one explain the absorption and exhalation in plants and animals which have no vessels, in the first period of organ formation, and in the formation of accidental tissues, by means of theories in which absorption is attributed to the lymphatic vessels alone, or at the most to veins . . . ? (19)

I suggest then, that it is to these proto-Positivists that we must look for the shift of the problem of absorption into its modern form, and especially to Foderà, who, associate of both Magendie and Blainville, managed to use this sophisticated biology in the context of experimental investigation. Such is my interpretation of the course of the absorption problem, and the entrance of the biology of tissues into the physiology laboratory.

It is no accident that the major French exponent of this tradition, Claude Bernard, was also a pupil of Magendie and attracted to the biological philosophy of Blainville. Bernard, in fact, began his research career by extending Foderà's experiments on absorption. Thus a great physiologist displayed clearly what a lesser investigator had begun to discern, from much the same standpoint (20).

DUTROCHET AND THE GENERAL PHYSIOLOGY OF ABSORPTION

Now I want to turn to Henri Dutrochet's work on endosmosis, for here, I shall argue, the general physiology of cells took its place in the laboratory. Dutrochet's results, coming soon after Foderà's work, helped in the programme begun by Magendie and Foderà. They suggested a possible mechanism for determining the direction of fluid movement, thus filling a gap in the physical explanation; they provided confirmation, if not explanation, of the fact that substances could cross tissues in two directions at once. Hence

if one looks at the mid-19th century literature on absorption, one finds endosmosis used within the framework of the problem erected by Foderà. Indeed, Italian historians of medicine have seen Dutrochet as formulating the laws regulating the movements discovered by Foderà (21). This, of course, is how Magendie wanted to use Dutrochet's work.

But to see Dutrochet's work as devoted to these ends would be to miss its rationale and to misread its context. For Dutrochet was not a young man in the Paris of 1826. He was not a new recruit to the task of applying physics to physiology. He was older than Magendie and he had been educated in Paris during the exciting period at the opening of the century when the physiology of the medical schools was strongly vitalist, when the Museum contained the materialism of Lamarck, as well as the more cautious attitude of Cuvier. Dutrochet's problem was not the connection between a slice of contemporary physics and an investigation of a physiological process; he was concerned with the older and wider problem of what constituted life.

Fig. 2. Henry Dutrochet, anonymous portrait, reproduced with kind permission from Joseph Schiller & Tetty Schiller, Henri Dutrochet (Henri du Trochet, 1776-1847) Le matérialisme mécaniste et la physiologie générale, Blanchard, Paris, 1975.

Dutrochet paid his respects to Cuvier, and to the caution of increasingly professional science, but given half a chance he reverted to the problem of the early 1800's; how to account for that form of molecular motion which was life.

Magendie, in 1809, just before his first absorption paper, in a purely theoretical paper, suggested that all phenomena of life could be reduced to the molecular movements of nutrition, and the action of the various organs. One day anatomy would be advanced far enough to see in the molecular organisation of the body parts the reason for their different vital actions, just as the different actions of the organs could sometimes be accounted for by their gross anatomy (22).

But how could one hope to unravel these secrets? One could invent hypothetical vessels and make them responsible for the selection of movement of different substances within tissues, but Magendie rejected this vitalist physiology of the schools. One could talk as Blainville did, of the analogies between life and chemical combination (23), but the model of tissues here was that of an almost homogeneous jelly; thus, even if one thought the microscope was worth looking down, one could not expect to see anything that would help one to understand the working of tissues. So one could appeal to the physics of materials, as Magendie did, or write reams on the chemistry of tissues, as Blainville did (24); but that was mostly a kind of anatomy-molecular anatomy, which was not yet explanatory, and was disconnected from gross anatomy.

Or one could do what Dutrochet tried to do: to investigate the workings of the tissues by progressive physiological analysis, relying on plant tissues rather than animal tissues, because only there was it possible to visualise the anatomical units clearly. By combining plant micro-anatomy with animal physiology, Dutrochet hoped to discover how animal and plant tissues worked.

Long ago, probably as a student in Paris, he had decided that plant/animal analogies could be very useful. When he had settled in Chateau Renault, he already knew a fair amount of botany. There, reduced to the same working conditions as the great 18th century experimental naturalists, he would be naturally led, like them, to study plants. Encouraged to experiment by his reading of Spallanzani, he dropped the "rational" physiology which had occupied him in Paris, the discussion of habits and sympathies, and devoted himself to the study of lower animals, plants and embryos.

There is no space here to ask why most of his work for the next 10 years was anatomical, nor why he only began his major series of researches in 1820. The answer would, I think, have to make strong reference to his friendship with Etienne Geoffroy Saint-Hilaire which began in 1817. Not that Geoffroy gave him the key ideas, but, I suspect, Geoffroy encouraged him in the rather adventurous physiology of the early 1820's, as he continued to be his champion in the endosmosis debates (25).

In any case, Dutrochet began to pursue his plant/animal analogies from morphology into physiology. From discussion of the oppositely arranged cortical and central systems in stems, he passed to an investigation of the opposite polarities of roots and shoots (26).

Further analysis of the supposed nervous substance of plants led to investigation of the sensitive plant, Mimosa. Experimental studies of the moving parts and the course of transmission, led Dutrochet to investigate the micro-anatomy of the parts involved. During these investigations, perhaps while attempting to characterise plant tissues by their reaction with acids, he discovered that heated nitric acid could separate plant vesicles. The separability of plant cells, reported earlier by certain German authors, was regarded as strong evidence against the view then common in France, that in plant tissues vesicles were formed as hollows in a continuous matrix (27).

At this stage, in 1824, Dutrochet produced his first published collection of memoirs, and in it he outlined a physiology of vesicles for animals as well as plants (28). In thus linking the two kingdoms of organised beings Dutrochet was following out a pattern long established in his research.

He was also linking his plant studies specifically with the then popular view that animal tissues were composed of globules of animal matter, especially albumen. But hollow vesicles were not semi-solid globules, whatever microscopical similarities might be claimed. Vesicles were a far more powerful model for the analysis of tissue function, for it was possible to apply the schemata of fluid physiology usually applied in connection with the fibre matrix picture of tissue structure.

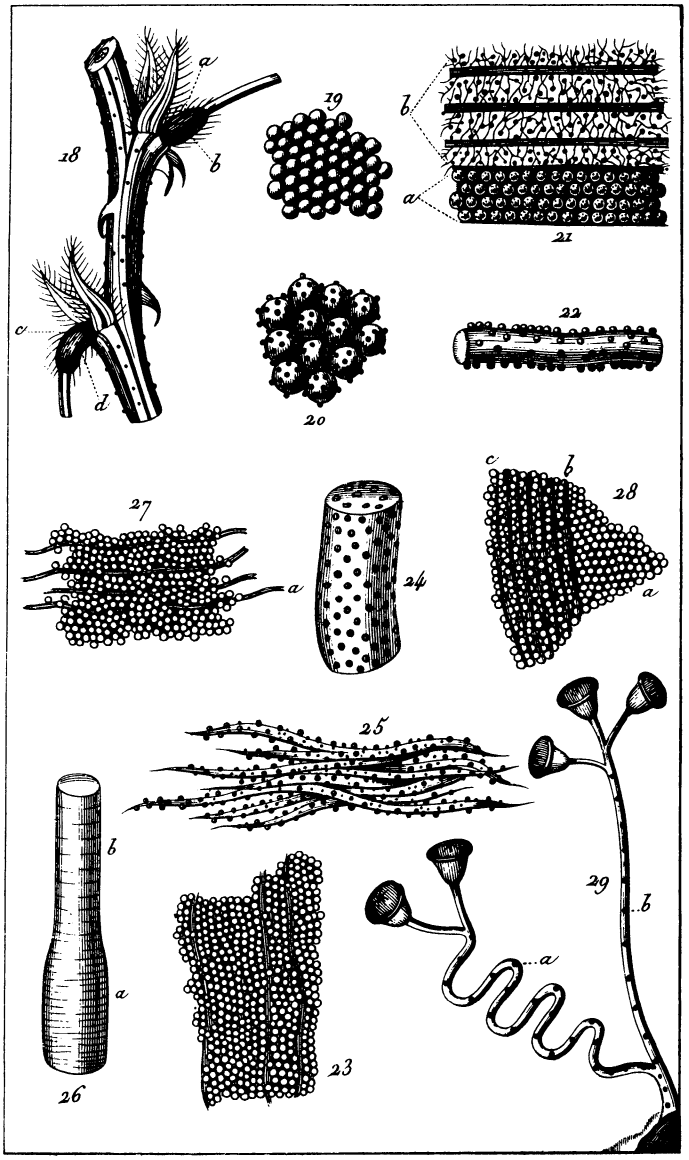

Fig. 3. **The microscopical structure of animal tissues according to** Henri Dutrochet; plate II, accompanying his Recherches anatomiques et physiologiques sur la structure intime des animaux et des végétaux et sur leur motilité, Paris, 1826. Note especially: fig. 21, nerve of Helix pomatia (snail), with globular sheath enclosing tiny corpuscules nerveux; 22, brain of Helix; 25, retractor muscle of Helix, fibrils bearing corpuscules musculaires; 28, heart tissue of Limas rufus (snail); note absence of fibrils. Fig. 24, part of an arm of hydra; 29, Vorticella.

It was then almost a platitude that vegetative life comprised the dual processes of composition and decomposition. Fluids were pictured as flowing through the tissue matrix, depositing certain materials, removing others. The active agents in some schemes, e.g. that of Bichat, were the vessels. They selected substances to be laid down or carried away. For Blainville, a sort of chemical affinity dominated. Dutrochet's physiology of vesicles had two considerable advantages. Firstly, discrete vesicles provided more definite sites for deposition. Secondly, the vesicle walls, acting as chemical filters, could serve to select the materials (29).

In some ways Dutrochet's treatment of vesicles resembled accounts in textbooks of fluid movement in larger cavities such as those of the joints. This notion that some vesicles secreted only material which was to remain within the cavity, or to pass into the blood, rather resembled the common treatment of such organs as the thyroid and spleen, which were thought to be glandular but which lacked excretory ducts (30). In fact, in much of Dutrochet's writing on vesicles, there is a stress on the hollow form, rather than on vesicles of a particular size range. As a physiology of vesicular tissues, it occupies an area between that of continuous tissues and that of individual, hollow, living units.

This vesicle theory, developed in 1824, was, one might say, waiting for the discovery of endosmosis. What Dutrochet knew of vesicles was precisely what he needed to know to apply osmosis; they were walled cavities, fluid filled. Thus endosmosis and exosmosis became the agents of composition and decomposition. A physical force had been uncovered which accounted for the movement of fluid into vesicles, and for a movement outward also. If endosmosis could be explained by electrical actions and so linked to nerve actions, then animal life, as well as vegetative life, could all be referred back to this immediate agent of all vital movement.

Dutrochet came to regret this initial, over-enthusiastic presentation of osmosis. He came to apply the phenomena in a more limited way, particularly in connection with plant movements, where the different cell size gradients in different parts of plants allowed the same osmotic force to explain various kinds of curvatures (31). But one ought not to dismiss the wilder applications of the discovery as momentary extravagances. In 1828, two years after his discovery, in presenting a new interpretation of the phenomena which involved active solids and active liquids, Dutrochet referred to supposed intra-capillary forces and suggested that the basic vital phenomena of contractility and sensibility could be so explained; a direct attempt to translate into physics the physiology then still taught in the medical school (32).

In further discussing Dutrochet's use of osmosis, I want to concentrate on the relationship, for him, of physics and physiology. It would be easy, from reading Dutrochet's final words on the subject, written in 1837, to suppose that his attitude was simply a physicalism more thoroughgoing than that of Magendie. He spoke of the phenomena of life being physical phenomena, exceptional not in their laws, but in the conditions of their occurrence. Vital phenomena, like metallic potassium, did not exist in the ordinary course of nature, but under certain special and temporary conditions, they could exist (33).

Dutrochet's attitude was certainly sometimes seen as anti-vitalist and therefore similar to that of Magendie, but this was not the only interpretation of their positions, nor the best, for it left only considerations of personal prestige to explain Magendie's animosity to Dutrochet's work on endosmosis. More perceptive observers saw here a wider difference of approach and one which rendered Dutrochet's work acceptable to many physiologists in a way that Magendie's was not.

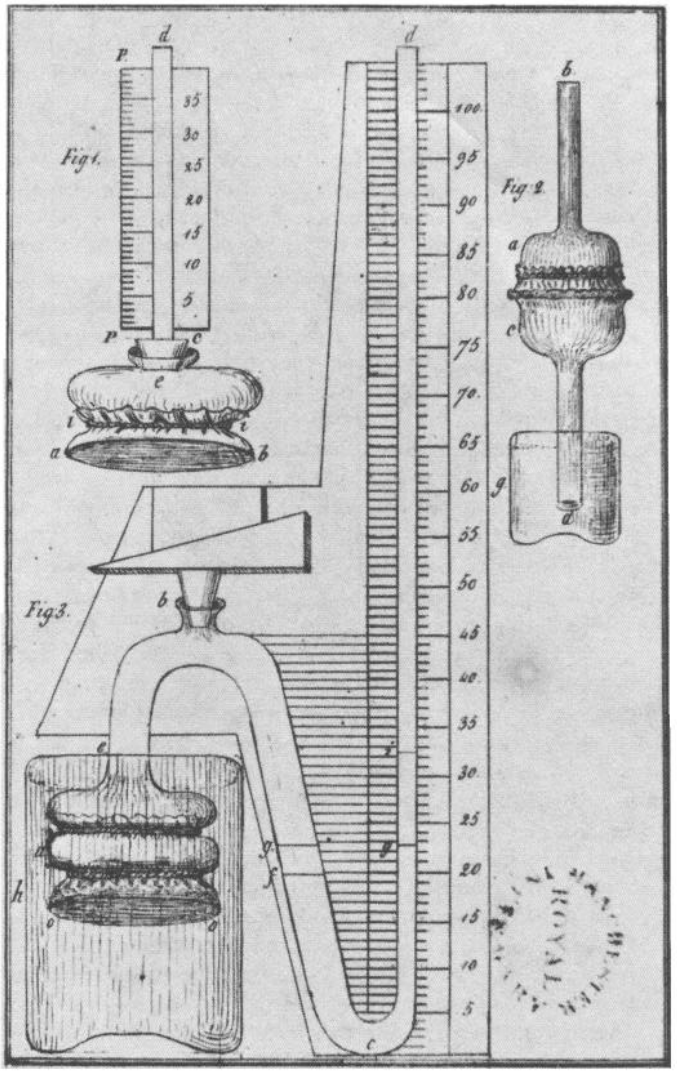

Fig. 4. Illustrations of Dutrochet's "endosmometers," from his Nouvelles recherches sur l'endosmose et sur l'exosmose . . . Paris, 1828.

We have suggested that Dutrochet reached his tissue physiology by a prolonged attempt at physiological analysis, pushed to the level of tissues. Osmosis fitted nicely into this framework as a physical effect characteristic of organised bodies. Dutrochet was at first convinced that it was in fact limited to organic membranes. When he later discovered that some inorganic membranes were active, no radical shift was necessary. Phenomena formerly restricted to organic bodies in principle, were now only contingently so restricted – in fact rather than by nature – because only in organised bodies was the relevant structure naturally found. For Dutrochet, the major difference between organised and inorganic bodies was that the former were vesicular, down to the level of the chemical molecules.

Dutrochet was seeking to uncover the physical phenomena characteristic of basic tissue structure. It is entirely appropriate that when he used inorganic membranes he was described as having recreated the phenomena of absorption in the mineral world. Magendie, you will recall, was accused of translating physics into physiology. The same difference in emphasis accounts for Dutrochet's search for new physics, contrasting with Magendie's use of contemporary knowledge (34).

As the vitalism of the French school began to fade and the physical sciences became more and more prominent in physiological research, Dutrochet's approach was seen by many as particularly promising. P. Jolly, for example, contrasted the vitalism of the French school with the attitude of Magendie (35). For Magendie, absorption was essentially imbibition; for Bichat and Richerand, absorption depended on the vital properties of the vessels. Dutrochet, however, while referring the phenomena of absorption to those of imbibition, demonstrated, none the less, that imbibition was the result of a vital faculty. In other words, Dutrochet preserved the distinctiveness of vital phenomena; his push to physics did not threaten the dismemberment of physiology in the attempt to hang it on the hooks of contemporary physics.

Indeed, Dutrochet hoped to locate the characteristic properties of life in the characteristic microstructure of the tissues common to all animals and plants. Where Foderà and Blainville pointed to the progressive complexity of the animal series, with the consequent range of properties, Dutrochet concentrated on what he saw as a common and accessible basic structure. I close with an extract from a contemporary review which underlined, and welcomed, Dutrochet's attempts to push physiological analysis to the level of a physics characteristic of organised bodies.

> But if in place of studying the topographical relations of a nerve, he [the anatomist] studies the intimate structure of nervous matter; if, in place of finding a canal joining two viscera, he finds in their molecular composition the immediate reason of their physiological operations; if he establishes by repeated rapprochemens, by ingenious comparisons, the analogy which exists between the basic forms and the diverse actions of organic substances; if, finally, he comes to be able to deduce, from this deep knowledge of the elements, the general laws of the masses, and thus to extract synthesis from analysis, will one then still call him by the same name, and will not the skillful workman be also, in this case, the most intelligent of architects? This is what M. Dutrochet has done.
>
> Thus what particularly distinguishes the works of M. Dutrochet, what stamps them with an original and particular character, is the intimate union, and, if I may say so, the continual fusion that he had known how to maintain between anatomy and physiology. Having once discovered the point of contact which connects these two divisions of the same study, he established there his scientific home, so to speak, and for more than fifteen years he has broken the virgin ground, whose inexhaustible fecundity he had foreseen (36).

When Magendie demonstrated the passage of acid across a vein wall in vitro, he was primarily interested in proving that veins would absorb. When Foderà, in extending this work, used sacs of vein, or gut, they represented convenient tissues, into and out of which various materials could pass. When Dutrochet used similar sacs, they represented not only the larger hollows of the body, they were, primarily, large, convenient models of the vesicular structure basic to all organised bodies. Movements of fluids in and out of the sacs represented the processes of composition and decomposition, and provided an insight into the mechanism and laws of this movement.

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DR. HARRY GOLDBLATT

Dr. Orr Reynolds received the following letter from Dr. David Goldblatt, University of Rochester, School of Medicine and Dentistry.

"Thank you for your expression of condolences on behalf of the American Physiological Society in the death of my father, Dr. Harry Goldblatt. Our family would like to inform the members of the Society that the Harry Goldblatt Fellowship in Cardiovascular Research has been created in his memory, under the auspices of the Council for High Blood Pressure Research.

We will appreciate the soliciting of contributions to the Fellowship. These should be directed to Mr. Jack G. Schmollinger, American Heart Association, 1689 E. 115th St., Cleveland, OH 44106."

NEWS FROM SENIOR PHYSIOLOGISTS

Richard Eckstein to Phil:

Thank you for your letter of greetings and inquiry. I have enjoyed reading the replies of others in The Physiologist and even though I was aware of a certain pride in the successful negotiation of 65 years, your letter added a definite feeling of pleasure.

I am still actively engaged in research on the aortic bodies which receive a coronary blood supply in adult dogs and have just had a manuscript accepted for publication in "Circulation Research." I also have a small practice in adult psychiatry. As far as I know now I'll be working for at least two years yet here at Case Western Reserve University. I have been interested in the fact that at this age I am doing more intricate work in my laboratory than I would have attempted years ago. I don't know whether it's because I'm more skillful or whether the magnifying glasses I need now make me more courageous. I suppose that miniturization is a sign of our times.

My health and that of my wife remain quite good and although at times the thought of retirement seems very attractive, at present our plans are not fixed and we'll await the future with interest and high expectations.

Eugene Robillard to Phil:

Since 1964 and until 1970, my functions as vice-dean and dean with heavy administrative duties, took me away from the laboratory and thus with regret I ceased to consider myself as a scientist. Since 1970 I am employed in the Division of Medical Education of the Professional Corporation of Physicians of Quebec. My actual interests brings me to read educational rather than biological literature. I am at times astonished to observe that in practice a same person demanding of himself a very strict scientific exactness in his professional and research work allows himself an uncertain attitude in his task as a teacher.

Paul Sekelj to Phil:

I am grateful that my physical and mental faculties permit me to carry on with some teaching and paper writing. Evidently not as strenuously as before. This applies equally to two of my favorite sports, fencing and skiing. More and more of my free time is spent in landscape painting, wood carving and repairing antique furniture. All these activities leave me little time and desire to worry about my future, since old age has no future. But there is a challenge, as Montaigue remarked, to retire successfully is no easy matter. I shall try to be reasonably successful.

With all my good wishes to you and members of the Physiological Society .

Roy Swank to Bruce:

Since my retirement two years ago I have continued to see patients. My interest is multiple sclerosis and I have been seeing more patients recently than I did while I was still an active member of the university staff. My office still remains in the medical school and I also have been able to maintain a small laboratory space where I do some research.

While I was on the staff I invented a first micro-emboli filter for transfusion in cardiac surgery. I have been deeply interested in this matter of blood-micro-emboli and have continued work on the filter. My own filter is being manufactured by Pioneer Filters. The general concept has been well received and now there are four competitors in the field. I am proud to say that we still have the most effective filter available.

John Welsh to Hal:

Much of my time has been spent in "tree farming". Although we are only five miles from Boothbay Harbor, a popular resort area, there are nearly 300 acres of timberland in the family and, with the help of the State Forest Service, we have been planting in old fields, having areas selectively cut, etc. We have a good market for pulpwood, logs and firewood so the improvements pay their way.

As a trustee of the Northeast Research Foundation, I have had a small part in establishing the Bigelow Laboratory (named for H.B. Bigelow – Harvard and Woods Hole Oceanographic Inst.) here at the Harbor. About 40 scientists, concerned largely with primary productivity in the sea, have made a fine addition to this community. These are in addition to the staff of the State Marine Fisheries Lab which is also located here.

Am also a trustee of the local hospital. So there is never a dull moment.

If you abstract a bit of this for The Physiologist I trust that you will quote me as recommending tree-farming as a fine way to spend one's retirement! I was 75 in August and still going strong!

Walter Fleischmann to Bruce:

I must apologize for returning your kind wishes somewhat belatedly but I had to go to the hospital for a brief but intensive treatment for bronchitis, which was quite successful, so I can resume my life as a retiree dabbling in music and horticulture and enjoying life. My sister and brother who both live in England flew over to be with me on my 80th birthday, which we celebrated quite cheerfully.

I enjoy reading "Perspectives in Biology and Medicine" (Univ. of Chicago Press) but must confess that much of it is over my head.

Curt Richter to Hal:

Your birthday greeting came today. Many thanks. It delighted me to hear from you and to know that you are having lots of fun. That goes for me too. I hope you will come to the American Philosophical Society meetings in April.

Edmund Jacobson and Bruce celebrate the same birthday, April 22. He remains active at age 89.

Our lab work is running merrily along: economics of human energy expenditure, computer run and computer measured.

Readers of The Physiologist will recall the many news items from Edward Allen Boyden who has been active in post-retirement research in the Department of Biological Structure, University of Washington. His friends will be grieved to hear of his death on Oct. 27, 1976. He was in his 91st year; his son writes that he died while working in his office. Having published three years of work on the monkey lung, he had received a four-year grant that would have enabled him to pursue his research.

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