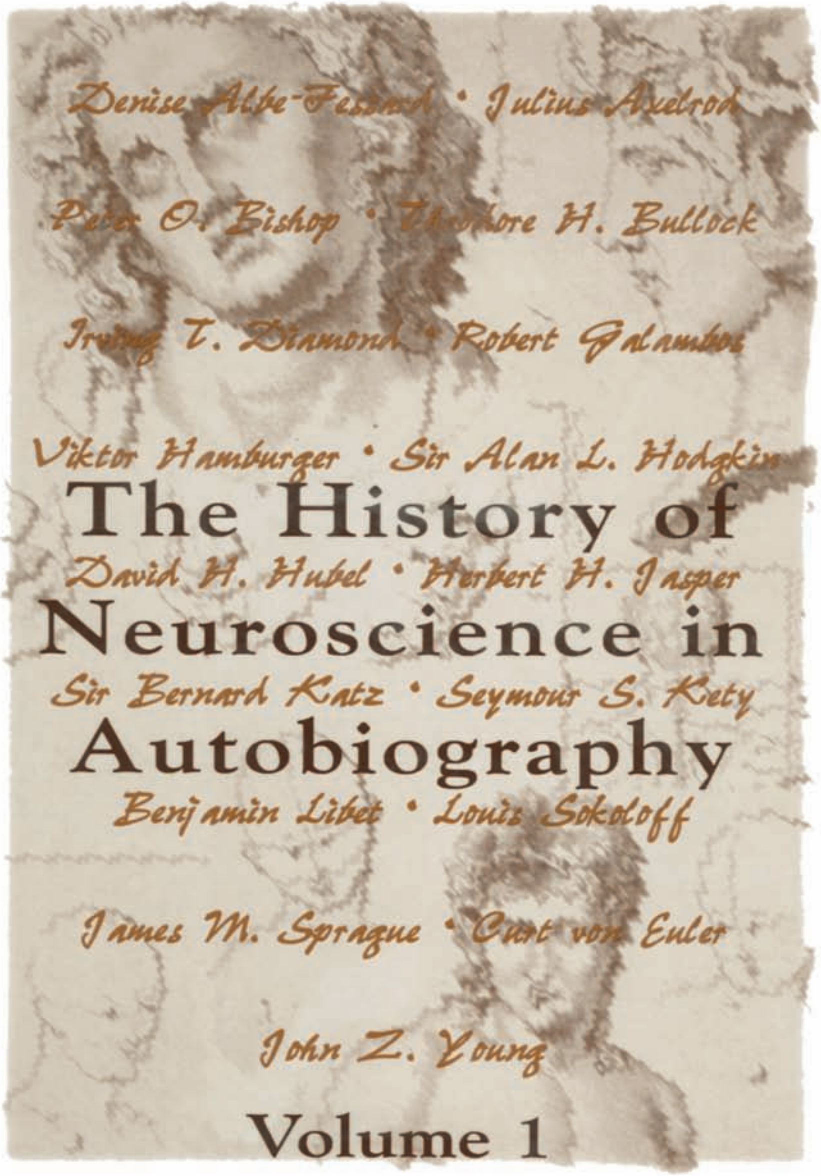


The History of Neuroscience in Autobiography

Denise Albe-Fessard • Julius Axelrod
Peter O. Bishop • Theodore H. Bullock
Irving T. Diamond • Robert Galambos
Viktor Hamburger • Sir Alan L. Hodgkin
David H. Hubel • Herbert H. Jasper
Sir Bernard Katz • Seymour S. Kety
Benjamin Libet • Louis Sokoloff
James M. Sprague • Curt von Euler
John Z. Young

Volume 1

Edited by Larry R. Squire

The History of Neuroscience in Autobiography

VOLUME 1

Edited by Larry R. Squire

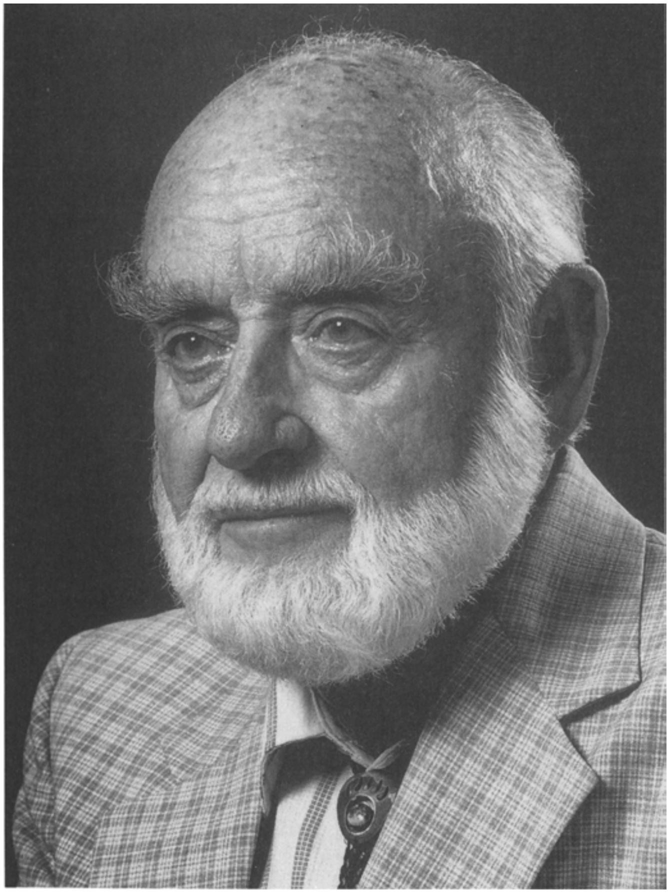
SOCIETY FOR NEUROSCIENCE 1996
Washington, D.C.

Society for Neuroscience
1121 14th Street, NW., Suite 1010
Washington, D.C. 20005

Printed in the United States of America.

Library of Congress Catalog Card Number 96-70950
ISBN 0-916110-51-6

Contents



Theodore H. Bullock

BORN:

Nanking, China
May 16, 1915

EDUCATION:

University of California, Berkeley, A.B., 1936
University of California, Berkeley, Ph.D. (Zoology, 1940)

APPOINTMENTS:

Yale University School of Medicine (1942)
University of Missouri School of Medicine (1944)
University of California, Los Angeles (1946)
University of California, San Diego (1966)
Professor of Neurosciences Emeritus, University of California, San Diego (1982)

HONORS AND AWARDS (SELECTED):

American Academy of Arts and Sciences (1961)
National Academy of Sciences USA (1963)
Karl Spencer Lashley Prize, American Philosophical Society (1968)
Ralph W. Gerard Prize, Society for Neuroscience (1984)

Ted Bullock has had exceptionally diverse research interests, from invertebrate neurophysiology to human electroencephalography. His interest in nonspiking electrical events led to the discovery of electroreception in fish, and his two volume treatise with Adrian Horridge, Structure and Function in the Nervous Systems of Invertebrates, *is the most comprehensive, authorative review of the topic ever written.*

Theodore H. Bullock

They tell me I was born on a sunny Sunday in May in Nanking, China, in 1915. I was the second of four children of Presbyterian missionary parents, Amasa Archibald Bullock and Ruth Beckwith. Before my parents met, my father had answered a call for Western teachers, published by the empress. He subsequently spent a year in Ch'eng-tu, in western Szechwan, teaching chemistry, his major subject at the University of California, Berkeley. In China, he fell in love with the people, their eagerness to listen, and their respect for learning. Finding a niche that suited him, he returned to the United States to take a master's degree in education at The University of Chicago and then to do advanced work in psychology at Columbia. His Berkeley roommate's sister was at Hartford Theological Seminary preparing to be a missionary, and father and she had corresponded but not met before he went to visit. In four days he secured her assent to return with him and spend a life in China. They left for China in 1909, honeymooning on the way for six months in Europe and India. Father joined the faculty of the University of Nanking to start its normal school and, among other activities, its program in agriculture. The still extant guest book of our home shows the signatures of Sun Yatsen, then president of China, and several members of his cabinet.

Most of my childhood memories center on a later home in the compound of the Central China Teacher's College in a village outside Wuchang. (In 1980 I had the thrill of finding that house, now a preschool, and the campus, now a normal school, well inside the metropolis of Wuhan.) Our home and schooling, while immersed in the native environment and with Chinese playmates, were as American as possible, to minimize problems when the children returned to the States. We returned in 1928, when I was 13, on my fifth transPacific crossing. A myriad of happy images and memories of the years in China are still vivid. Are they filtered by time? Do they account for leanings and bents—such as feeling like a citizen of the world first, of the United States second?

My parents were Victorian in social mores, conservatives economically, but liberal religiously and politically. My father certainly encouraged curiosity and a spirit of inquiry (misprinted in one book dedication to him as "the spirit of iniquity"); mother just wanted us to do anything well. My older cousin Mary Beckwith was a spinster and a serious amateur conchologist. Over Christmas of 1926 she had us at her house in La Jolla, California (where, 40 years later, I returned to stay) and got me started in shell collecting. Back in central China I collected freshwater and terrestrial shells in kitchen middens and on ivy-covered walls. To identify my prizes I took them to the museum in the British Concession in Shanghai, when we sought refuge there for some months while Chiang Kai-shek drove up from the south through Wuchang. In Berkeley, while attending Garfield Junior High School in 1928, I recall pedaling downtown on my bicycle and buying cowries (*Cypraea* spp.) from an eccentric dealer on Shattuck Avenue to add to my collection.

Two phases of high school years in Los Angeles and Pasadena were especially influential. Pasadena High School and Junior College was a combined school of high standard, and several biology teachers encouraged student research projects as well as participation in instruction. I learned a wide range of histological microtechniques and became particularly familiar with the Cajal and Del Rio Hortega methods for silver and gold impregnation of neurons, astrocytes, oligodendroglia, and microglia in normal rat brain and after needle wounds. Slides of these stains are still in my collection along with many later ones and some historic gifts from classical microscopists. The first tangible evidence that I might have some ability was a prize given by my teachers, a stimulating 1908 book on comparative histology by Dahlgren and Kepner. Pomona College had a marine station at Laguna Beach and admitted even a high school student to the summer session. Over four summers I took marine biology and other courses as well as student research. One project that gave positive feedback was methylene blue staining of the nerve plexus in the pharyngeal wall of amphioxus. Crustacean muscle nerves stained easily; sea anemone and starfish nerve cells or fibers never stained.

The hardest nugget of this writing project has been to find the words to answer the question, why am I doing science; what was the basic motivation? It would be much easier to pass over this tricky bit of self analysis, letting the record speak. Something makes me try, anyway, at the risk of being misunderstood. The fact is that when I first began to think about vocations, I wanted to belong to something with a large and nonmaterial purpose. I thought a lot about the church, the foreign service, or a world organization. I remember the inspiration of a youth congress on comparative religions of the world and the respect for others that it inculcated. A second requirement arose later, as I became aware of what people do in various jobs. I found I wanted something where the demand is to be creative, with the limitation between my ears, rather than what has been planned by others or comes to the door or fits within guidelines. I envied composers, architects, and city planners. Although occupations involving service to people had a certain pull, the greater tug had been those that offered more scope for discovery. It wasn't that I always wanted to work with animals. But a decisive influence, suggesting research and teaching in zoology, must have come from the happenstance of a generous relative, cousin Martha Beckwith, sister of Mary, who made possible the summer course just mentioned, in the same year that my biology teachers were encouraging me in independent projects. This plan dawned, withstood tests, and turned out to fit the bill; it has been everything I could wish for in challenges, satisfactions, human contacts, and the possibility—ever present though faint—that something one does may be significant.

With an associate in arts (A.A.) degree from Pasadena Junior College, in 1934 I went to the University of California at Berkeley for my junior and senior years, majoring in zoology. On the side I worked on a large termite research project under the protozoologist C.A. Kofoid, making slides of the rich fauna of protozoans in the termite gut. One of Kofoid's pet ideas was the "neuromotorium" he had described in advanced ciliates, a silver-stained spot supposed to coordinate the rapidly switching ciliary beating of different clusters of cilia, according to the microsurgical experiments of C.V. Taylor on *Euplotes*. When Wally, a favorite elephant of the children of San Francisco, had the misfortune to step backwards and kill his keeper, he was duly condemned and executed with postmortem rites performed by the chief of pathology at the university, who handed out bits of the elephant's tissue to ranks of scientists waiting with bottles of fixatives. Kofoid sent me with a preheated Thermos bottle of hot Schaudinn's solution to get fresh material from the caecum, where giant heterotrich ciliates live, sporting spiral membranelles and, presumably, the best of all neuromotoriums. When I returned to the lab and found I had preserved this valuable material in hot water, having neglected to replace it with Schaudinn's, I expected the earth to open and swallow me up. Luckily, Kofoid left for a collecting trip to the antiquarian bookstores of Europe and months later could see my error in its true perspective—or this chapter would never have been written.

It was a long breath hold, in 1936, applying for a teaching assistantship in competition with many others from across the country. Luckily I landed one and within a year Martha Runquist and I were married on the $500 per year salary. In the third year I was elevated to chief teaching assistant and stepped up to $550 per year, so we both bought new shoes. Among many others, some of the teachers and courses I remember were S.F. Light on invertebrates, R.M. Eakin on general zoology, J.A. Long on embryology, Richard Goldschmidt on cytology, S.C. Brooks on general physiology, J.M.D. Olmsted on mammalian physiology, H.M. Evans on the history of biology, Joseph Grinnell on vertebrates, Stanley Freeborn on insect morphology and insect physiology, and John Gullberg on microscopy. Among my near contemporaries I can mention only a few: Aubrey Gorbman, Fred and Avery Test, Olga Hartman, Bill and Mollie Balamuth, Bob Fernald, Morgan Harris, Frank Pitelka, Norman Kemp, John Mohr, and Mimi Stokes James. I did my thesis with S.F. Light on the anatomy and physiology of the nervous system of a group of invertebrates, the enteropneusts, in the days when the dissertation was an unpublishable tome; it was four years before my last chapter was published. Ever since, I have pressured my students to submit the thesis in the form of chapters ready for submission, if not already sent, to a prestigious journal.

This is a story about ideas: thinking of them, re-examining them, formulating them for teaching to beginners or to postdocs, selecting them for investing research time—all within a defined domain of natural science. Sustained thought, reiterated questions, the rigorous boundaries of logic and evidence, the ever-present demand for controls and explicit effort to disprove, a tremendous dependence on the subjective component, on imagery and imagination—these converged on a limited number and range of particular issues. Still, there have been multiple themes. Besides transient phases, I have chosen to arrange these reminiscences around the warp and woof of a few main threads and leitmotifs of the scientific interests I indulged in over many years. Some are explicit sections; others are not treated separately. Some biases will be obvious and may rear their heads more than once. A penchant for the relatively neglected issue, technic, or animal group and avoidance of the popular one can be discerned. I am certainly not the one to interpret this—is it fear of competition or love of prospecting? Of course, I rationalized it as the latter and perpetrated a preachment, one Friday night at the Marine Biological Laboratory (MBL) in Woods Hole, Massachusetts, on the need for prospectors in the face of the gold rush of popular, reductionist cell biology. I have also preached on the need for more comparison of taxa, particularly the phyla and classes representing major grades of complexity of brains, and the need for descriptive exploration of the phenomenology they manifest—natural history, in the best sense. In a recent, invited piece I have already recounted many of my memories about controversies and quiet revolutions in brain science at the middle ("mesoscopic") levels of integration that lie between ionic channels and psychological phenomena (Bullock, 1995).

Family and Off-Campus Life

My choice of families was fortunate on both sides. I have said my parents were supportive; they understood and appreciated teaching and encouraged my bent for scientific research. My two brothers were both in commercial research laboratories, my sister was a nurse, and they each brought choice in-laws into the circle. The sizable Runquist clan on Martha's side was salt of the earth and made me feel accepted, although my occupation, beyond teaching, was hard to explain. Martha and our two wonderful children made our home easy to come back to and hard to leave so often; their unquestioning patience was an undeserved miracle. The pleasures of bedtime reading, singing around the piano, camping, school open house, and going to visit one or another grandma and grandpa meant a lot more to me than the share of my time they got. I enjoyed puttering in the garden, terracing the slope, fixing things at the level of drip irrigation systems, and raccoon-proofing the garbage pail. As a superb cook and thoughtful hostess, Martha made legends I still hear about from friends around the world with her buffet dinners and Christmas parties for graduate students and visiting firemen. The community Methodist church was an important part of life, Martha being a professional staff member while I got as far as committees on social concerns and the Amnesty International chapter. Although our churches have been what is conventionally called liberal theologically, it is a mercy that I have not had to explain my own beliefs; I'm sure some of our dear friends would be shocked at the level of scientific humanism. I'll come back to home and family again, but here begin to overview my research interests.

An Anatomical Leitmotif

Although I cannot claim substantial, original contribution, an interest and respect for structure reappears over the years and had a strong influence on my thinking. At first—that is, in high school—my anatomical interest was in making specialized technics work for silver and gold staining of neurons, astrocytes, microglia, and oligodendroglia. These methods had been published by the then still living Spanish anatomist, Santiago Ramón y Cajal, who shared with the Italian Camillo Golgi, the first Nobel Prize in anatomy. By about 1930 I was a student in Pasadena, fascinated with the more challenging histological stains. When I succeeded with these, the idea took hold of seeing for myself the reported changes in microglia with time and distance from a needle stab wound in the cortex of a rat. When this also succeeded I screwed up my courage and took the interurban train to the giant Los Angeles County Hospital to visit the neuropathologist, Cyrus Courville, whose name I had encountered in the literature, to consult him about both glial stains and the Marchi method for tracing connections of myelinated tracts. I still have the 65-year-old slides I made showing corticospinal fibers decussating in the rat medulla and fewer but scattered fibers in the pigeon spinal cord after lesions in the cerebrum on one side. What made an impression on me as a junior college kid about that visit was listening to the great pathologist dictating his observations to his secretary in perfectly formed sentences while doing his brain slicing of the postmortem specimens of that week. In 1951, he again did me and others a service by publishing the English translation of *Cajal's Precepts and Counsels on Scientific Investigation, Stimulants of the Spirit,* with advice on how a scientist should choose a wife and a project.

Most of my anatomical forays have been done with collaborators. I looked, sketchily, at the giant fibers of many polychaete annelids, including some of their synapses. Wade Fox joined me to describe the remark-able sensory nerve endings of the infrared receptors in the facial pit of pit vipers, and was aided by lucky silver impregnations. Elizabeth Batham and I examined electron microscopically the infoldings in the larger axons of the sea slug, *Aplysia.* I encouraged my student, Ellis Berkowitz, to collaborate with electron microscopists and apply their tool to verifying the absence of true, tightly wrapped myelin sheaths in the spinal cord of lampreys (Schultz et al., 1956). Before saying too confidently that these sheaths are not to be found in agnathans, perhaps invented in some corner of the brain or trigeminal roots, I persuaded Jean Moore to join with Douglas Fields and look again, at many levels and at the much better brain of hagfish. They found the absence complete, implying an invention of true myelin in ancestors of modern elasmobranchs, who have abundant, well developed myelin sheaths. The principal evidence of my appreciation of anatomy, however, is in the studies of many students and postdocs who took my advice and supplemented their physiological contributions with proper anatomical controls. Some went on to do major morphological work on their own or with my laboratory neighbor, Glenn Northcutt. This appreciation of anatomy also led to chapters in my books and had a profound influence on my speculations, for example, about the evolution of complexity and of the number of kinds of nerve cells.

A Thread of Research on Nerve Nets

Having chosen for my Ph.D. thesis a G.H. Parker-type study of an obscure group of worms, significant mainly for being the lowliest creatures to have been listed at one time among the chordates (our own phylum), it was not a great surprise but rather welcome news to discover that these worms have a nerve net. Nerve nets are well developed in jellyfish and their cnidarian relatives but elsewhere, from flatworm skin to mammalian gut, are generally absent, not properly demonstrated, or conduct only locally. Nerve nets are the simplest form of nervous organization and may coexist with a centralized nervous system, but this is unusual.

Nerve net is a well defined term, established in the last century, for a certain form of nervous organization to be distinguished from a peripheral plexus or tangle of nerve fibers. The main criterion of a nerve net is diffuse conduction, that is, spread of excitation from any stimulated locus to any other place, even after incomplete cuts anywhere, as though the conduction system is netlike and lacks essential pathways like nerve, which are bundles of parallel fibers. Nerve nets are quite different from a popular object of study today, called neural nets (better spoken of as neuroid nets), which are principally models in computers. The term neural net is also sometimes applied to local assemblies of cells in gray matter with unknown connectivity.

My interest in nerve nets focused on how we can account for a diverse repertoire of behavior in cnidarians (jellyfish, anemones, corals, and others) with the known properties and anatomy of the nervous system—an interest we call today neuroethology. This was a direct extension of the work of Carl Pantin (1935) who believed that he could more nearly account for the known variety of movements of sea anemones, local and general, spontaneous and responsive, than could be done for any other animals by the variety of dynamic properties of junctions. Jellyfish have quite another lifestyle and my first aim, at Woods Hole in 1940 and in Pensacola, Florida, during the first few weeks after the Japanese attack on Pearl Harbor, was to compare jellyfish with Pantin's story on sea anemones. This project worked out well and the next step, a bizarre one for me, was determined by a conversation with David Nachmansohn, then also a visiting investigator at Yale. He believed the acetylcholine mechanism, with its specific enzymes, was important for both conduction and transmission, intracellularly in both axon and synapse, rather than only extracellularly at synapses. I agreed to provide material for chemical analysis from various invertebrates and spent hours picking out the caprellid amphipods from, seemingly, bushels of the colonial hydroid, *Tubularia*, to purge the cnidarian of advanced arthropod molecules. Cnidarian and other taxa proved to have the cholinergic machinery, and I became a party to a vigorous debate in the literature about the role of acetylcholine in conduction. The debate simmered for decades after I left it to return to integrative and organizational questions. I have not heard that the case is closed yet! Nerve nets continue to fascinate me and receive intermittent attention at long intervals.

The next major advance was in Robert Josephson's thesis (1961). He not only did novel experimental physiology in a new group, the colonial hydroids, but with the help of computer and modeling experts designed a digital model based on the most realistic anatomy and physiology. The model was used to extend the efforts of Adrian Horridge (1957) to account for the diverse forms of spread of excitation in coral colonies within the known parameters of cnidarian nets. Up to the present, this has not been accomplished, but we have not given up because even these simple and randomly distributed variables offer a large range of permutations to test (probabilities of synaptic connection and of requirement for facilitation). This was dramatically shown in a Ph.D. thesis under Michael Passano at the University of Wisconsin by David Smith (Smith and Bullock, 1990). Smith found a critical combination of parameters in a model that can, in a computer, spread excitation not around corners but only in straight lines, as I had found in 1965 in the skin of sea urchins and declared to be inexplicable with familiar nerve net organization! In the meantime, the Josephson, Reiss, and Worthy model had been improved and used in a satisfyingly affirmative test of the question whether such randomly constructed nets can show preferred (most effective) temporal patterns of stimulation (Fehmi and Bullock, 1967). At this writing I am hopeful about a newly programmed model that might permit more thorough tests of the range of responses of cnidarian-like nets. The capabilities of primitive nets and of the variables we know about are still not appreciated, especially when one adds degrees and distributions of spontaneous patterns and of superposed modulation by a second net. I am confident that true nerve nets and realistic models of them still have much to teach us.

Postdoctoral Years at Yale and the MBL at Woods Hole

When I finished the Ph.D. requirements in 1940, a postdoctoral year of further training and pure research was uncommon. The traditional goal for the relatively privileged was a period in Germany, England, or Scandinavia but these opportunities were closed; Europe was already at war. I was extremely fortunate to be awarded a Sterling Fellowship in zoology at Yale. Before reporting to J.S. Nicholas in New Haven, my mentor in the Osborn Zoological Laboratory, I spent the summer at the MBL at Woods Hole on Cape Cod. The next summer, Martha and I went again to the MBL without knowing where we might be in September but, luckily, a Rockefeller Fellowship in neurophysiology under H.S. Burr at Yale came through just in time.

Four years at Yale and summers at Woods Hole were formative and influential. Besides meeting a wide cross section of people in zoology, physiology, anatomy, and related fields, the opportunities to learn new techniques, especially electrophysiological ones, and to apply them to simple invertebrate preparations were golden. I became imprinted on comparative physiology and on the importance of combining anatomy and physiology, on the value of simple systems, and on the diversity of integrative mechanisms in the nervous system. At brown bag lunches, teas, or seminars, I came to know Alexander Petrunkevitch, Ross Harrison, Evelyn Hutchinson, Dan Merriman, and Grace Pickford, among others in zoology and H.S. Burr, Ralph Meader, Warren McCulloch, Harold Green, John Fulton, Leon Stone, and others in the medical school.

Other lifelong influences, already strong at Berkeley and enhanced in New Haven, included an appreciation for the history of science. In 1943 Yale gave a prize to the medical student with the best list of errors found in Vesalius' epochal *De Humani Corporis Fabrica,* on its 400th anniversary. I developed a deep respect for the reservoir of information in the older literature, which at that time meant pre-1925 and especially late 19th century, when the profusion of scientific journals was hardly 50 years old. Confession being good for the soul, I must underline how handicapped I have always been by failing to gain a level of working proficiency in German and French, although we had to pass exams for a so-called reading knowledge in both, and I had to read and distill thousands of papers in the normal course of business. Later I have felt bad not knowing Spanish—all the worse because the smattering that sticks is so useful and so much fun, as was the smattering of Portuguese, Italian, and Serbo-Croatian I picked up on working visits to Amazonia, Naples, and Yugoslavia.

After a few summers at Woods Hole I was invited to join the teaching staff of the historic course in invertebrate zoology at the MBL (1944–1946). Later I was invited to take charge of the course (1955–1957), selecting 55 students from a long list of applicants, plus nine staff members, assigning the phyla, choosing the destinations of the boat trips for field work and the captains who timed each of the teams' turns on a succession of stations. The organization of this complex course went smoothly, but that was about as close to administration as I ever got. Although not inclined to buy a cottage in Woods Hole, we returned many times over the years and it is heartwarming to see our grown children eager to visit the haunts of their early years and show them to our grandsons. I was particularly honored to be asked to return in 1991 as Alexander Forbes Lecturer for the second time, after 28 years.

Early in 1942, just settling in to the Rockefeller Fellowship, I was recruited into a war research project on mustard gas prophylactics and antidotes and, by the summer, into teaching gross and neuroanatomy under the wartime pressures of accelerated production of medics. I had a rather obese cadaver all to myself from which to learn gross anatomy a few weeks ahead of the students, in a small, top-floor room during the hot months.

A Thread of Research on Slow Potentials

No doubt this recurrent motif originated from the major research concern for direct current (DC) fields of my second postdoctoral sponsor, Harold S. Burr of the Yale anatomy department. I was never much excited by the steady potentials seen between virtually any two points on the surface of the body, whether plant, hydroid, or human. I did find it intriguing that a salamander egg became electrically quite busy with fluctuating potentials after several cleavages. The hypothesis of Gesell (1940) seemed both plausible and heuristic: that DC fields can influence the level of excitability and of spontaneous firing of neurons, whether the field is extrinsic or, as he proposed, also intrinsic—a standing potential difference between the dendrites and the axon. In any event, I developed a permanent interest in the intercellular effects of DC and slowly changing fields.

Such effects appealed to me, for one reason, because they pointed to the possibility that besides individual impulses and synapses, other means of communicating are possible between cells or from the synchronized population to the individual cell. The notion of field effects on neighboring cells is still current, exciting, and unproved, although a strong case can be made from direct evidence under artificial conditions and indirect evidence under normal conditions. I first attempted to test the notion by polarizing the semi-isolated cardiac ganglion of *Limulus*, a thread-like concentration of cells on top of the heart that drives the neurogenic rhythm. Lifting the ganglion off the heart allows a weak electric current to modulate the rate of heartbeat command discharges. I found that both polarities caused acceleration, and I had to fall back on the explanation that the large number of ganglion cells are oriented in various directions and those excited by the current win out over those that are slowed down.

We needed a smaller ganglion. Fortunately, Alexandrowicz (1932) had described the cardiac ganglion of crayfish and lobsters as having only nine cells. Of these, four turned out to be pacemakers and oriented predominantly the same way. This preparation speeded up the heart rate in one direction of polarization and slowed it down in the other. But it was some years before we knew this because my first attempts to prepare the lobster heart so that it maintained a normal beat failed. Only after Donald Maynard joined the laboratory to do a thesis on this ganglion and brought his skill to bear did this and other experiments succeed, opening a new window on integrative properties of neurons, to be discussed below under that rubric.

Still later, with Carlo Terzuolo, we pushed the sensitivity of nerve cells to DC a notch higher by using the tonic stretch receptor of the crayfish abdomen. Extracellular fields of only 50 μV across the cell sufficed to accelerate or decelerate, according to the polarity. This preparation permitted intracellular penetration, but it was not surprising that we could see no change in the membrane potential during an imposed change in firing rate—for two reasons. One is that, in our uniform field configuration, all the current entering the cell on the anodal side of its electrical equator must leave it on the cathodal side, hyperpolarizing one region and depolarizing the other. These regions might be out in the processes, whereas the soma where we penetrate might be close to the equator. A second reason is that the membrane potential of this pacemaker cell is constantly in flux by millivolts, and a few microvolts will be difficult to see, even by averaging. Electroreceptors, as we learned shortly, can be up to several orders of magnitude more sensitive still, but not to DC. They are tuned to a best frequency which in some species or organs is a fraction of a Hertz, in others up to 5,000 Hz.

Low frequency electrical connections between cells, quite unlike electrical synapses tuned to millisecond presynaptic impulses, were found in the lobster cardiac ganglion (Watanabe and Bullock, 1960). As mentioned elsewhere (see Neural Integration Thread), the ganglia electrotonically spread slow potentials directly from one cell to another, not through the extracellular compartment. This nonconventional form of communication might occur quite widely without having been detected. Because of that possibility I consider this discovery to be particularly important. It represents one member of a family of forms of communication between cells unlike the orthodox synaptic form; the family includes electrical and chemical field effects of shorter and longer range, even perhaps physical effects, such as pushing or dehydrating, which are playing roles of unknown proportion in the recesses of the brain.

In view of this highly speculative bet (a more accurate term than theory or hypothesis, which have become so fashionable as to be overused in the competition for attention and grants), this may be as good a place as any for the following remark. I believe the pervasiveness of the subjective element in the process of doing science is often overlooked but can hardly be exaggerated. It works both ways—that means it often works against us. Many times I have felt like reminding discussants that what seems patently obvious to them in formulations, priorities, and weighing of evidence seems patently different to some other, also presumably informed individuals. Beyond the ordinary undervaluation of areas we do not appreciate is an unfortunately common undervaluation of other scientists in our own area. Without elaboration, I simply refer, with regret, to the many cases I have known of ad hominem antipathy based on no scientific argument but real or imagined behavior. Less ignobly but more widespread and insidious: how much more real and hence weighty is the evidence we have seen for ourselves than the other fellow's evidence, which we have only read. Less common is the overconfidence of self-recognized authorities, particularly in the hard sciences—which can spice up a colloquium amusingly. One has led a sheltered life who has not heard some exchange like this, in the question period after a seminar by a famous visitor:

"Unfortunately, your algorithm is inapplicable under those conditions, on basic physical principles."

"Thank you, I meant to make it clear that we and our physical-mathematical consultants have shown that it is indeed applicable."

"It happens that I am knowledgeable in this field and the laws of physics and simple math definitively exclude it."

"Very sorry, you must be overlooking Spandau's recent reanalysis."

"On the contrary, I...."

But, of course, subjectivity is not to be avoided—it is the root of the new idea and the basis of the motivation to follow through. These facets need no comment from me.

What I am told would be interesting to some readers is my own, highly subjective view of the goals of neuroscience, the strategies, fads, and discouragements of its researchers and the outlook for different approaches. One hears "What is it going to take? Do we have to work out every synaptic coupling strength, every channel time constant in each cell, and all the subcellular parameters before we can test the adequacy of our understanding with a realistic model? What constitutes understanding? How are we going to formulate a general theory of the brain?" My reaction is that I am excited about the opportunities in unraveling how brains work, despite the serious obstacles to general models and theories, because I see our knowledge as so preliminary that further revolutions are the only certainty—at least as drastic as those we have already experienced. I expect these revolutions to occur independently in each field—chemistry, anatomy, physiology—and each level—molecular, cellular, small assembly, and multilayered system—as they have in my lifetime (Bullock, 1995). The goals and opportunities I see as most heuristic, at this stage in our science, are not great simplifications, like the neuron doctrine, or great interdisciplinary cooperations, like anatomy and behavior in the brain imaging of active areas during cognitive tasks—significant and satisfying as these advances are. The most heuristic opportunities are rather discoveries of new entities, relations, dependencies, and proportions—natural history or phenomenology of the organized assemblage of neural tissue. All my experience leads me to expect that major novelties will turn up, as they have year in and year out, each opening new windows and multiplying the degrees of freedom. To reiterate a small part of a long list of such findings within not so many decades, witness graded synaptic potentials, lateral inhibition, presynaptic inhibition, gap junctions, nonsynaptic electrotonic connections, corollary discharge, multiplicity of modulators, multiplicity of channels, kindling, face-selective cells, and plasticity of cortical maps. These are permanent advances; models and theories can be helpful in recognizing the next measurement to be made but are almost certain to have a transient vintage. For many purposes I have found that analogies stimulate ideas for new measurements—like the crowd at the stadium as an analogy of assemblies of nerve cells. To the complaint that I am only adding intricacy and minutiae to an already impossibly complex task, I can only answer, that's the way it is and it can only get more so. Who can say what is unimportant? Within the vast area of our inadequate information base, an especially conspicuous dimension is ignorance of the relative importance of the known variables. I feel keenly that at least the generalists and the theorists, the modelers and the synthesizers should remind themselves often that our enormous knowledge of nervous systems is still extremely primitive. Hence my optimism and sense of adventure—there is greater opportunity than anywhere else I can imagine for solid new discovery, from elementary fact to broad principle, from subcellular to cognitive level, from simple to complex grades of evolution, from early to mature and aged stages, and from normal to pathologic states. We are not suffering from lack of a general theory but lack of simple facts—mostly due to technical difficulties.

I present these remarks early to avoid their being anticlimactic near the end! They may seem abstract or worse here, without the bases that many later sections provide. I will return to some more specific comments on strategy in some of those sections.

Neural Integration Thread

An interest in the multitude of ways that output as a function of input can be varied, within and among neurons, has particularly appealed to me, perhaps because it gives the feeling that one is finding out something intimate and solid about how the brain works, especially how it evaluates and compares. My first summer in Woods Hole, in 1940, when I chose to extend the crude experiments of my thesis on the enteropneust nerve net to jellyfish, I used the methods Pantin (1935) had introduced with sea anemones—basically just single, controlled shocks and isotonic recording of the strength of response. His discovery of junctional facilitation impressed me with its simple elegance and power to explain widely diverse behavior by differing time constants of build-up and decay. An integrative property of this name was known to Sherrington and others at the reflex and higher levels but not at the synaptic level, probably because it did not happen at the healthy neuromuscular junction of frogs and cats. Wiersma and Van Harreveld (1938) found facilitation highly developed and differentiated among different crustacean neuromuscular junctions. I found (Bullock, 1943) that this simple dependence on the amplitude of the last contraction and the interval to the next one can account for about 85 percent of the fluctuation in strength of jellyfish swimming beats, leaving 15 percent to free will!

At this time the local potential, discovered by Bernard Katz and Alan Hodgkin (references in Bullock, 1995) in crab nerve—a subthreshold, graded, nonlinear response within a few millimeters of the stimulus—was under debate. It seemed to me a good candidate for a postsynaptic explanation of the inferred state of facilitation. What caught my attention, especially in 1946 after watching the labile subthreshold responses of the single giant synapse in the squid (before the first intracellular junctional potentials of Paul Fatt and Bernard Katz), was the multiplicity of apparently independent variables that must converge to determine output as a function of input. Accommodation can be small or large; afterpotentials can be in either direction, each small or large; cells can be more or less iterative, more or less regular; some are sensitive to temporal pattern at a given mean frequency of arriving impulses, others not; some are spontaneous and others not; firing rate can be a steep or a shallow function of depolarization; excitability can vary independently of responsivity. All this was before the discovery of the host of synaptic variables that continues today to grow with each year's journals. Summarizing our understanding, I listed 48 variables like the seven just given, in a textbook (Bullock et al., 1977). There are workers who recoil from this enumeration as hopeless complexity or who become engrossed with the ultimate explanation of one or another property in terms of ion channels and third messengers. My choice has been the approach of the naturalist anxious to know all the phenomena nature presents and their occurrence and dependencies, before dismissing any as trivial. This choice led to studies of similarities of axons and synapses in some of these integrative properties, sense organs as models of synapses, fatigue and subnormal responses as models, quasi-artificial synapses, the distinction between excitability and responsivity, and specializations in certain axons that are tolerant of stretch while maintaining conduction velocity with decreased diameter.

An intracellular phase began in 1955 with the indispensable skills of Susumu Hagiwara. We worked first on the squid giant synapse I had exploited extracellularly, then on the lobster cardiac ganglion, a miniature model of a brain, with only nine cells. These nine cells include pacemakers showing spontaneity and pattern, and follower cells that filter, integrate, and amplify their input. These preparations underline anew the permutations of integrative variables.

As in other phases, post- and predoctoral co-workers were vital and immensely rewarding friends—in this case, besides Hagiwara, there were Carlo Terzuolo, Takuzo Otani, and Akira Watanabe. Akira brought a new dimension, not only to us but to neurobiology, when he discovered the direct electrical connections between neurons in the lobster cardiac ganglion. Subsequently, we showed these connections can usefully spread slow and sustained subthreshold potentials between cells, electrotonically, but cannot propagate or transmit impulses (see also A Thread of Research on Slow Potentials, above). My contribution was to suggest the experiment to show that these connections can provide a nonspiking feedback from follower onto pacemaker cells, whereas no synaptic feedback has been found in this preparation. This and other new integrative variables led me to formulate the locus concept, expounded in a review in *Science* (Bullock, 1959). This concept underlines the idea that the subthreshold activity in a neuron is local and distinct in its various parts, such as the one or more pacemaker regions, terminals of separate axon branches, and discrete afferent dendritic regions. Each part is a site of integration and possible lability and plasticity. I began to add the evolutionary dimension in 1958. In 1961, stimulated by our first recordings from electrosensory afferents in electric fish, I began to think of the variety of forms of signaling between cells as coding principles, both in the domain of nerve impulse trains and in the nonspiking mode.

It should not be surprising that the brain, the most complex system known (apart from systems of brains), has many degrees of freedom. Just because a McCulloch-Pitts model (McCulloch and Pitts, 1943) or another one made of limited kinds of units and variables is believed, in principle, to be able to do anything, it does not follow that the brain works that way. Fishing for new principles of operation in real brains is surely one of the most rewarding routes to new discovery about what evolution has accomplished in the nervous systems of animals. Modeling subsystems or operations of the brain is today the fashionable thing—and I cheer and support those willing to join the hunt, with whatever weapons. Modelers underline that they have to select the variables that seem important and simplify or standardize the many others known to exist, on the assumption that the latter are not important. I cannot help pleading, over and over, that we have no proper basis for selecting and should keep open other variables from the long list known. Especially important, we should undertake more descriptive exploration for new phenomena in wet brains. I am sure we have yet to uncover major surprises. "Classical" synapses, for example, may not be the overwhelmingly important form of interaction between cells that we confidently assume.

My own involvement in neural integration moved up from single synapses and intracellular views of single integrating cells to simple interactions like the results of repetitive trains of inhibitory (J.S. Schulman) or excitatory (J.P. Segundo) impulses on a pacemaker. The elementary case was the tonic stretch receptor of crayfish, where anomalous acceleration from inhibitory input manifests phase locking and provides one of the best examples of a biological value of "noisy" irregularity, better called useful jitter.

The reports of Wiersma and Waterman, beginning in the mid-1950s, of units in the optic lobe of lobsters and crayfish that respond selectively to natural stimuli with a combination of visual features, began a whole new chapter in sensory processing and brain operations that has interested me much more than my meager contributions to it would suggest. From personal observation of the experiments of Jerry Lettvin and his colleagues on similar units in the frog optic tectum in 1957, I became convinced of their reality and their importance for brain physiology, although these two propositions had a long uphill road to general acceptance and still have not found a real place in the prevalent models of sensory recognition.

My own experience was interesting. Aspiring to contribute to what I perceived as an exciting new field, in 1959 I proposed to my visiting investigator from Germany, an established expert in central visual units, that we try to find the units that Lettvin and company had reported in the frog tectum, in order—if we could confirm their reality—to add quantitative detail. These units respond well only to small objects or contours, preferably darker than the background and sharp edged (focused), moving within a 5° excitatory receptive field, in the absence of too much movement in the surrounding inhibitory receptive field. He demurred, saying it was a flash in the pan and would soon be found to fit into the scheme of ON-center, OFF-surround units known from the cat retina. Perhaps out of respect for his host, he offered to allow his wife, Ulla Grüsser-Cornehls to waste time on this wild goose chase if she wished. But this adept and dedicated worker could not find such units! I telephoned Jerry and he promptly flew to California, showed us how, and found the units within minutes in the first preparation. After that, Ulla (Grüsser-Cornehls et al., 1963) had no difficulty and published papers for more than 25 years on these complex recognition units, actually retinal ganglion cells or their tectal endings. These units and counterparts in higher, cerebral levels, such as the face-selective units and others in the primate temporal lobe, and song-specific units in cerebral nuclei in finches remain in need of both reductionist analysis and assessment of their normal role and adequacy to explain behavioral recognition. Clearly small sets of nearly equivalent complex recognition units that need not fire in particular spatiotemporal patterns do exist. No one proposes that this solution accounts for all or most recognition, but ideas are needed for uncovering what classes of stimuli they do operate upon.

I find neglected and hence attractive the compound activity of organized groups of cells and their complex electrical signs. New levels of integrative mechanisms require exploration—synchronization, quadratic phase coupling of nonharmonic frequencies, population thresholds, and the like. Obviously I subscribe to the tactical rule that we cannot wait for an adequate understanding at simpler integrative levels before plunging into investigation of more complex levels (see EEG and EP/ERP Compound Field Potential Thread).

I have argued that the standard concept of the brain as a system of circuits has long been inadequate, except as a first approximation. Adding up to something far different from any accepted meaning of "circuit" are a number of whole categories of features of neural systems, especially the more advanced levels of them. The known variety of geometric configurations of axonal ramifications and dendritic arbors, making the functional contacts not a 1-μm electron microscopic specialization, but a defined spatial array of them, is one category. Field effects, electrical and chemical, of various degrees of diffuseness or intimacy form another category. The variety of transmitters and modulators and their specific distribution within as well as among cells is a third category. The great variety of integrative properties characteristic for each locus, plus extensions of them like the kind of nonsynaptic, slow electrotonic communication described above, may be considered a heterogeneous fourth category. Some of the integrative properties overlap with Pasko Rakic's "local circuits," for example, nonspiking neurons. These are well known in invertebrates and in the retina and are highly likely in vertebrate brains. Even more likely is the transmission of graded influence between spikes.

I reject the criticism that this catalogue of variables is an appeal to a hopeless complexity; it is a call for more effort to assess what is really going on, more descriptive natural history, before assuming that familiar circuitry with impulses and classical synapses is the main and adequate principle. Consider the retina. Better known than many other systems, it is still full of such noncircuit dynamics as induced rhythms, traveling waves, and temporally precise expectation waves (omitted stimulus potentials, OSPs, see EEG and EP/ERP Compound Field Potential Thread).

Giant Systems Phase

In the 1930s and for decades thereafter, the giant fibers of earthworms, crayfish, squid, and many teleosts were nothing more than an extreme specialization for some advantage, like an elephant's trunk or tusks. We focused on giant fibers as accessible cellular units, hoping their membrane and synaptic properties were not too specialized to teach us general physiology. Each had had its dramatic history of discovery and debate as to whether it was vascular, supportive, or neural. My own interest was not so much in the cellular and membrane mechanisms as in the organization of the afferent and efferent system and the integration at giant synapses. That interest began with the 5-μm fibers, giants relative to all others, in the wormlike hemichordates.

Earthworms were more interesting, having two complementary chains of syncytial units with septal synapses and afferent connections only from the front end to the median chain and from the tail end to the lateral chains, plus efferent connections to anchoring bristles that cause a pulling in of the head end when the median system is excited or of the tail end when the lateral system is excited. The system was unique, too, in that the single impulses in a true physiological unit could be recorded in the intact, behaving animal. I spent some time in the early 1940s developing a circular race track carved in paraffin and covered with a glass plate, in which an earthworm could crawl while we electrically stimulated and recorded from several places, permitting quantitative measures such as conduction times to be followed day after day in the same unit, during acclimation or other treatments. The arrangement worked well, but I failed to make any publishable discoveries! The earthworm's marine relatives, polychaete annelids, were interesting for other reasons, mainly because of the extreme diversity, among families, in the development of giant fibers and of the nervous system as a whole. The diversity made them the most valuable group for arriving at a plausible view of the biological meaning and behavioral correlates of giant systems, with confirmation from work with crustaceans, cephalopods, teleosts, and others, including odd groups like phoronids and lungfish.

The function of Mauthner's fibers in fish had been debated for many years. I well remember the day a paper came out in *Nature,* reporting that African lungfish have unusually large Mauthner's axons. I sent out to the tropical fish store for a specimen, and Don Wilson found that he could record impulses in a single axon firing to a gentle tap from the surface of the intact animal, independent of escape movements. It appeared that giant fiber systems are not so much escape mechanisms as startle response devices and that saving time by fast conduction is not as important as synchronizing a widespread musculature.

University of Missouri at Columbia, 1944–1946; UCLA, 1946–1966

With two postdoctoral years, I qualified for the title of instructor at Yale in my third year. I felt lucky to be offered an assistant professorship at the University of Missouri Medical School in 1944, to teach first-year gross anatomy and second-year advanced topographic and applied anatomy to the medical students, and anatomy cum physiology to prenursing students. At that time a two-year medical school, Missouri required a relatively heavy teaching schedule, but I enjoyed it and in addition was able to do some research.

Good fortune intervened again when I landed a job in 1946 at UCLA in my own field of zoology. I enjoyed teaching the introductory course, Zoology 1A, as well as advanced invertebrate biology, with student projects in physiology and experimental ecology. As a university, UCLA was young and malleable then, so that some of the committee work was interesting and actually brought about innovation—academic senate bodies, the new medical school, the life sciences building and its sea water system, the Brain Research Institute (BRI), and later the Molecular Biology Institute, departmental planning and recruitment, and the local chapter of the American Association of University Professors, of which I was president from 1955 to 1956.

I learned three things in these UCLA years. (1) A complex organization such as a university, having evolved procedures and rules for every situation, is in constant need of individuals who will propose new precedents. (2) Everybody agrees that inadequate communication is a root cause of much of the world's grief, but few apply that insight to their own situation. (3) Always send carbon copies to everybody you can think of. The same and a few other diplomatic lessons helped out in dealings with the American Physiological Society, the American Society of Zoologists (of which I was president for a term and a half in 1964 to 1965), the Neuroscience Research Program (in which I served as chairman of an advisory committee to the director at a crucial period) and its work sessions and intensive study programs, the National Academy of Sciences (NAS) (where I served as chairman of the Section of Zoology during the time of its dissolution and served in the same capacity in the newly created Section of Neurobiology), some divisional and program committees of the National Science Foundation (NSF), and study sections and two councils of the National Institutes of Health. In those days there was relatively better communication on some matters; for example as a recent and raw recruit, I had to stand in front of the NAS membership and speak for the election of a fairly controversial nominee, as was then done for every nominee.

Although my own research was focused on comparative neurophysiology at the level of the synapse or a simple circuit of neurons, I supervised Ph.D. theses and postdoctoral projects in physiological ecology, mainly in temperature acclimation, until the field became too large for me to follow in addition to the expanding literature in neurobiology—about 1963. This interest led to serving on several committees, including the Environmental Biology Panel of NSF, under George Sprugel, Ladd Prosser, and Dwight Billings, and participating in some expeditions, such as the second resurvey of Bikini and Eniwetak atolls, right after the first hydrogen bomb test in 1948.

To equip and protect my first graduate student, Robert Lindberg, who studied the field biology of the California spiny lobster, I had to provide not only face masks, hoses, and a portable air compressor light enough to launch in a skiff through the surf, and later, a self-contained underwater breathing apparatus, but also the first rules in the University of California for the safety of divers.

During those years our daughter Chris and son Stephen were growing up in Pacific Palisades. Martha drove millions of sorties jitneying them to countless activities, the vector sum of which eventually led to satisfying careers for all. The line between home and science was often fuzzy, as when bags of rattlesnakes hung in the garage. During car-pooling with two additional families, the long-suffering kids were a captive audience for many a long-winded answer to what they thought was a simple question; so they grew up patient and tolerant.

Courses and Teaching: Graduate Students and Postdocs

If the threads of research were the warp of the fabric, the woof was teaching, which enriched and invigorated me from 1936 to the present, with only sabbatical interludes. Perhaps a better metaphor would be an emulsion, with teaching the continuous phase and research the discontinuous phase. Much of the pleasure and challenge—not often commented on—is the daily range from dealing with beginners in structured settings (college courses) to graduate students doing theses, postdoctoral learners acquiring self-confidence and independence, and senior visiting investigators from East, West, North, and South. In the latter category I count well over 100,* and I have supervised 34 doctoral students. They have been particularly close friends, bearing and forbearing for five years or more, on average. Many and diverse have been the graduate student weddings Martha and I attended. I feel fortunate that most of my students went through the system before the current fashion for qualifying exams that hardly go beyond a defense of the proposed thesis—a concession to specialization that reduces the incentive to breadth in our future teachers and scientists.

---

*Space does not permit listing them or citing theses and publications. A bibliography can be found in Bullock (1993a).

I began teaching as an occasional invited expositor and tutor at Pasadena Junior College for my teacher, M.W. de Laubenfels, while I was a college freshman. At Berkeley the zoology department took seriously the inculcation of high standards of preparation by TAs for every laboratory exercise and oral quiz, and conducted training sessions of two or more hours weekly. I either took or conducted these sessions every term from 1936 to 1939. In contrast, the medical students in anatomy courses at Yale were "treated as adults" and left largely on their own, with a cadaver, books, a partner, and easy access to instructors but no required examinations for two years. I enjoyed both systems and, at UCLA, both the large elementary classes and small advanced classes. In the large, lower-division zoology classes I had full responsibility for the schedule, labs, field trips, and TA training. In the advanced classes I experimented with project-oriented lab courses, inspired by the MBL experience, and still have a great file of project reports in invertebrate comparative and ecological physiology, which have been a gold mine for thesis proposals.

Even the core medical school courses and still more the elective courses at the University of California, San Diego (UCSD) gave scope for experiment. I recall arranging with Sir John Eccles, then in Buffalo, New York, to stand by for a call. I then answered the expected student question after my lecture on the cerebellum, "Let's ask Eccles what he thinks." I dialed him and the class talked directly to him over a speakerphone. I was one of the few lecturers who used the autoscoring machine—with a set of buttons at each student's place—to ask a few questions at the start of the hour and another few at the end; this worked well with carefully prepared questions. With graduate students and postdocs, phases of experimentation have been rampant—tutorials and written propositions, journal clubs, a "Peripatetic Seminar in First Principles," and a cooperative "Neurological Study Unit," often planned with Bob Livingston, plus neuro-campouts, tide pool trips, and Friday afternoon conferences on everything.

My course in scientific communication has run for 28 years and was a direct outgrowth of courses in scientific writing I attended in Berkeley in the 1930s, given by Joseph Grinnell, and in Los Angeles in the 1950s, given by Victor Hall. I broadened the scope to making the transition from student to professional, including use of the library, history of scientific communication, the roles of scientific societies, verbal and poster contributions at meetings, the preparation of illustrations, grantsmanship, letter writing, informal communication, ethics, the academic marketplace, and communication between scientists and the public. For some years Theodore Melnechuk was my coinstructor and brought a broad and unique experience in many areas. More recently, Glenn Northcutt has joined me; in addition we have an invited expert at nearly every meeting. Many are the opportunities to advise, admonish, and inculcate, giving examples from experience. One troublesome topic has gradually become more difficult—who should be coauthors, and how should this be determined? It is not much help to pronounce, realistically, that practices differ among laboratories and to advise open and early discussion. The upward spiral of numbers of coauthors cannot long continue, but what counterforces will emerge to resist the inflationary pressures for coauthorship, which go beyond any reasonable attribution of real authorship or ability to defend the propositions?

Science is an acutely historic process because one always wants to know what's been done and what's not been done. The privilege and good fortune of being able to do science, to profess research, to think hard and long about what needs to be done, and then do it, write about it, and lecture about it is so vividly real that one almost feels guilty of self-indulgence, enjoying life more than one deserves. It is hard, however, to accept the fact that one's work, far from definitively correcting the mistakes or inadequacies of the past and adding valuable new understanding, will become the flotsam and jetsam of the moment, soon to be passé and in a shorter and shorter span, forgotten—within 25 years, not even cited. I know. I have both experiences every day.

Add to that the enormous and nearly ever-present pleasure of dealing with other people—co-workers, students, and seniors—on a plane of the most satisfying level, mutually appreciating creativity, daily and hourly seeing improvements or advances, seldom distracted by personality clashes, rivalries, or profits and losses. "Exciting" would be the most overused word if we used it for each occasion that deserved it—dozens of times per week in a normal period of lab work, journal reading, phone calls, e-mail with colleagues around the world, and coffee breaks with co-workers. All the synonyms in the thesaurus apply now and then, some only once a week, like electrifying or delighting, others maybe once a day, like intriguing or fascinating. One might even call it a sensory-enriched environment such as keeps old rats' dendritic spines turgid.

Physiological Ecology Thread

This phase of activity, lasting through most of the UCLA period, was an alternative area for graduate theses and postdoctoral projects; I was deeply interested in comparative physiology of ecological import and particularly, temperature acclimation (Rao and Bullock, 1954; Bullock, 1955, 1958a), but confined myself to synthetic papers. Some of the issues and ideas are mentioned in A Technical and Mathematical Leitmotif. My first graduate student (R.G. Lindberg) chose a field study of the southern California spiny lobster and others studied osmotic (W.J. Gross) and hemocyanin (J.R. Redmond) problems. Most, however, carved out aspects of adaptation to habitat temperature (J.L. Roberts, P.A. Dehnel, E. Segal, P.E. Pickens). Postdocs K.P. Rao and O. Kinne measured responses to salinity and temperature in a number of taxa. H. Barnes concentrated on cirripedes and their feeding, metabolism, respiration, and behavior in relation to salinity, ions, general ecology, and distribution.

The interest in ecological physiology was a natural result of my upbringing in invertebrate zoology, which always included living material and, whenever possible, field work, and of my later focus on physiology, which came largely from teaching experimental invertebrate biology at the MBL and comparative physiology at UCLA. The story of a boost from field and aquarium studies of an unexpected behavior in limpets is recounted in the section Behavioral Thread. A number of expeditions to do neuroethology on the coral reef, at the Japanese seashore, in the Amazon, in the Gulf of California, and elsewhere whetted my appetite for more contact with the field. Service on a number of national committees dealing with ecology meant acquaintance with many leading ecologists of a generation now largely gone. The impossibility of keeping reasonably informed in this field, as well as in neurobiology, compelled my retreat from active engagement in it by the mid-1960s but did not quench an amateur interest, which has been continuously stimulated since then by having ecological lab neighbors of a yeasty ilk at the Scripps Institution of Oceanography (SIO).

Expeditions and Field Work

The MBL at Woods Hole taught me that even moderately complex electrophysiology could be done by packing up everything, down to the last screwdriver, setting up in a day or two, even in damp rooms on simple benches, if only the jellyfish, worms, squid, or rays are available. Visiting marine stations or making our own temporary laboratory in a shed on the shore, my students and I learned how to ask Brazilian collectors in Portuguese for unusual electric fish, how to catch baby sharks on the mid-Pacific reef with a Polynesian throw net, how to look for a school of squid in Monterey Bay at night by the faint glow of the luminescence they stir up from the microplankton, and how to repair Ampex instrumentation recorders on deck under the tropical moon. The unexpected became the norm as we worked—for a few weeks every hundred or more weeks—at Pacific Grove, Plymouth, Naples, Friday Harbor, and similar civilized stations, and at Bikini atoll, Barro Colorado Island in Panama, a tiny zoo in Belem, Brazil, a public aquarium on the Izu peninsula in Japan, a billfisherman's cottage near La Paz on the Sea of Cortez, and a former sea captain's house in Kotor, Yugoslavia. Among my co-workers, the lesson came harder to some—always be flexible and ready to adapt, but be sure to get reportable answers to significant questions in a short time. My own experience has been only about two dozen such expeditions but I surveyed systematically the experiences of several hundred scientists who worked, in the first few years of the SIO Research Vessel (R/V) *Alpha Helix*, on short-term physiological and biochemical, anatomical, and behavioral operations in remote locations, most of them without previous experience of this kind. The findings were surprisingly favorable in terms of published output but underlined the requirement for imaginative improvisation.

A Technical and Mathematical Leitmotif

Any claim under this motif seems out of place from one with such limited training in the basic disciplines of hard science. I have always felt these weaknesses keenly and occasionally made a commitment to devote the time to rectifying one or another, but failed to follow through. I have neglected not only mathematics but chemistry and molecular biology, the hallmarks of today's neuroscience. Surprisingly, I have found that practical biophysics and some applications of mathematics are approachable with little more than concept and intuition, plus guardian angels in human form who protected me from the more egregious errors. One such expert was the electronics engineer who drew me a circuit for a pulse-generator-stimulator in 1941 when no such item was on the market; I learned some basic electronics building that circuit, discovering only at the end that we had both forgotten to include an on-off switch.

Electrophysiology took an early postdoctoral grip on my fancy, thanks to kind hosts at Yale, where I divided my time in 1940 to 1941 between the laboratories of J.S. Nicholas, embryologist in the zoology department, and H.S. Burr, electrophysiologist in the anatomy department. I was introduced to electroencephalographic (EEG) recording and evoked potentials (EPs) by watching Warren McCulloch, Clyde Marshall, and Les Nims conduct strychnine spike neuronography in monkeys. This is a method for finding direct cortico-cortical and cortico-subcortical connections, and was introduced by the team leader, Dusser de Barenne. After a 72-hour experiment, the team was pleased to accept my offer to clean up, which gave me the opportunity to learn the knobs and dials, record spikes and brain waves from monkeys, and pick up some of the black magic and pitfalls of electrode preparation and placement.

I never got over the wonder and excitement of seeing a green streak on the cathode ray oscilloscope (CRO) that betokens a real, living response, hence a connection and a congeries of dynamic properties between the site of stimulation and the recording electrode—subject to a myriad of artifacts and misinterpretations that suggest, in their turn, control experiments and more fun. The opportunity is infinite for devising procedures, and one must be as interested in results as in improvements to avoid the common syndrome of instrumentation fixation. When four-gun cathode ray tubes became available, before good, high frequency electronic switching, we rigged a standard, single-gun CRO for such a tube and enjoyed four-channel recording, the start of a permanent passion for simultaneous observation at many places. The first and last paper for which I was paid ($25, as I remember) described how to calibrate camera shutters with a CRO.

Frustration stimulated the cathode ray direct-recording caper, which had to do with the difficulty of choosing between two means of recording. The CRO had to be photographed, with consequent delay for developing before seeing results. The moving mirror oscillograph, from which recording paper came out developed, could not follow frequencies high enough to record nerve impulses faithfully. I journeyed to DuMont headquarters in New Jersey and was encouraged to try my idea of collecting the cathode ray beam at the screen, on one of a row of wires and delivering it, after amplifying the current, to one of a row of pins fixed over a strip of moving Teledeltos (electrically marked) paper. DuMont gave me an empty glass cathode ray tube, the glass blower at Yale sealed into the screen the row of platinum wires, DuMont installed the cathode ray gun and sealed the evacuated tube—and I failed to confine the collected current to one or two wires! Another idea was based on a new kind of cathode ray tube with a high-frequency spinning beam (hundreds of kHz) and a circle of collector wires, announced by a small spin-off company of DuMont. I visited them and proposed to gate the cathode ray current at the same frequency as the rotating beam to record a DC signal on one wire and to frequency-modulate the rotation for AC signals, the collector wires feeding a row of pins marking a moving strip as before. This plan for a direct-recording high frequency oscillograph sounded good to the company, who said they would try it, but I never heard of it again.

When I invented a way of continuously displaying spike intervals-vs-time (by condenser charging—long before digital computers) and told H.K. Hartline that we called it our PIP, for pulse interval plotter, he said they had something of the kind, hitherto unnamed—and christened it, on the spot, his time interval totaler.

Besides devices and procedures, something has made me get involved in relatively neglected quantitative natural history, from extremely simple projects to those well over my head but intuitively promising. One example is the comparison of temperature effect ("Q_{10}") at different temperatures and after acclimation. Another is the comparison of extent of temperature acclimation possible among different physiological processes in species from different habitats and latitudes. I came to the view that animals are not just a collection of molecules and structures but as much a bundle of rates that have to be in harmony—one cannot for long have more egestion than ingestion. Different rate functions often acclimate to different degrees, some more than others. The reason, so I proposed, that all animals don't live everywhere, by acclimation, is that in poor acclimators, the rates get out of harmony. These examples come from projects in my ecological physiology period (see Physiological Ecology Thread).

In the area of sensory physiology, I became intrigued with the comparison of sensory receptors, pacemakers, and neurons generally, with respect to their regularity and distribution of interspike intervals as a function of the mean frequency of discharge. Although a strong tendency is widespread for regularity to increase as mean frequency rises, relatively as well as absolutely, cells are not all alike. A wide variety exists, from clocklike cells to jittery and extremely sputtery ones, compared at a common mean rate—and I still have no idea why. Two extremes are the highly regular pacemakers in the brain of certain species of weakly electric fish that command electric organ discharges (EODs) with a standard deviation of intervals 0.01 percent of the mean (100 times smaller than classical "clock" cells) and the highly irregular infrared receptors of rattlesnakes that maintain a spontaneous background with interval variation several times the mean. I believe we still have a poor empirical knowledge of the distribution of these properties among species, parts of the brain, stages of development, and extrinsic influences—as with most others of the dozens of "personality" properties. Further natural history is needed at least as much as models based on inadequately informed simplification.

The last example of this urge to quantify, even to the point of getting in over my head, involves the closer description of the structure of activity in brain waves, as I explain later.

Sensory Physiology Thread

Herpetologists R.B. Cowles and K.S. Norris (subsequently known in cetaceology) pointed out to me in 1951 the facial pit of pit vipers and the conclusion of the latest papers that it might be a sense organ detecting a slight warming of the air by warm-blooded prey. On a lucky guess that nearby trigeminal nerve branches supply the pit, we anesthetized a rattlesnake and found heavy traffic of spontaneous activity in the steady state, without intentional stimulation. Simple tests showed that purely radiant heat suffices to enhance and radiant cold to suppress this activity, independent of the intervening air temperature. As a sense organ, it was fascinating for several reasons. One is that the spontaneous discharge of each afferent unit is extremely irregular, leading us to speculate that perhaps several subthreshold oscillations of different frequencies arise in separate sensory terminals and add, like local potentials, in a nonlinear fashion to cross threshold irregularly. Regularity becomes both absolutely and relatively greater as stimulation drives up the mean discharge rate. A second aspect of general interest is the problem of explaining the high sensitivity. The possibility of a wavelength-specific photochemistry could be virtually excluded and instead a high sensitivity to temperature change of the nerve terminals could be directly shown—extending to a few millidegrees centigrade, providing it happens rapidly. This may not be much different from the sensitivity to temperature change in the sensory terminals of our face but the pit viper sensory membrane requires a millionfold less caloric flux to raise the nerve ending temperature that much—because the sensory membrane is small and barely 15 μm thick, with an air space behind it. The nerve endings are directly under the 2 to 3 μm-thick epidermis. The physiology and light microscope anatomy occupied several years and got me hooked on sensory physiology as a window onto neural processes.

A 1952 visit by Yasuji Katsuki, the prominent auditory physiologist, led to the second sensory sally—into the lobster statocyst, then called an otocyst. Because hearing is uncommon among aquatic invertebrates and stimulation with acoustic signals has tricky artifacts, I was wary of doing experiments myself. With Katsuki's expertise and the able assistance of a student, Melvin Cohen, we soon decided this organ was not really acoustic, and Mel went on to do a thesis on the variety of things it really does.

Yasuji also told us his idea, based on the properties of lateral line receptors in fish, that some sense organs have dual channels. One set of receptors has thin afferent axons, low thresholds, low slopes of the intensity/response function, more tonic responses, and larger receptive fields. The other set of receptors has thicker fibers, higher thresholds, better intensity discrimination, more rapid adaptation, and smaller fields. In a literature survey, I found evidence of a similar dichotomy in nine cases, ranging from earthworm giant fibers to mammalian lung mechanoreceptors—not justifying a rule, but a common example of parallel channels for distinct aspects of information processing.

Electroreceptors were unknown but called for by the ingenious experiments of Lissmann and Machin on a weakly electric African fish in 1958. We guessed the afferent fibers might be in the lateral line nerve and soon found a place where the right branch is just below the skin in common knife fishes from Amazonia. With my skillful colleagues, Susumu Hagiwara, Kiyoshi Kusano, and Koroku Negishi, we readily isolated single fibers, and two important discoveries emerged. First, the afferent nerve fibers respond not only to feeble electrical gradients, they respond to naturally occurring electrical events of biological significance to the species, namely the EODs of the same fish, as distorted by either conducting or dielectric objects, such as other fish or stones, and the EODs of other conspecifics. Hence, the receptors can be called electroreceptors. Second, some of the afferent fibers in species with sustained, regular, ca. 300 Hz EODs follow those EODs one to one and encode useful information, not by any change in maintained impulse discharge rate but by a maintained shift in phase (precise to a fraction of a degree) relative to the EOD and other afferent fibers. Other fibers encode by a change in their probability of following; that is, they miss some cycles of the EOD and fire on other cycles, within 20° or so. This was the clearest evidence that besides the classical frequency-of-impulses code there are other nerve impulse codes. We spent some time defining several of the codes and reviewed the subject with the late Donald Perkel (Perkel and Bullock, 1968).

In addition to these first two surprises, others cropped up. One was the sharp tuning of these EOD-sensitive receptors to the particular EOD frequency of each individual fish and the ringing oscillation of the receptor at that frequency, when stimulated with a brief square pulse. Another was a whole class of electroreceptors that is stimulated not by EODs but by slower fluctuations, below ca. 30 Hz, largely because of ventilatory and locomotor movements of skin and gill generators of sustained leakage currents in the same or other fish. This finding opened up the possibility, subsequently confirmed in many families of siluriforms, and in sturgeons, polypteriforms, lungfish, and others, that many nonelectric fishes and even lampreys can have electroreception as a distinct, specialized sensory modality—as Kalmijn had shown for nonelectric rays and sharks, and later workers showed for a number of urodele amphibians.

Some evolutionary surprises are mentioned later in the section EEG and EP/ERP Compound Field Potential Thread. I always thought of electroreception as interesting, not only as a unique modality some taxa have and we do not, but also as a source of general principles. Because such sense organs have evolved not once but several times (see Evolutionary and Comparative Thread), could there be central neurons sensitive to microvolt or fractional microvolt fields within the brain itself? Even if the sensitivity is only to tens or hundreds of microvolts, this possibility would mean the larger brain waves and EPs and many of the little-studied ultraslow potentials could normally influence firing probabilities or cause transmitter release without impulses. A long list of features known only or particularly well in electroreceptors is given in an edited volume on electroreception (Bullock and Heiligenberg, 1986). These features include ultrastructural changes with activity, tight junctions far from the equator that make asymmetrical voltage drops across apical and basal membranes, resonance of receptors and its plasticity, and the meaning of efferent innervation of receptors. Similarly for central features, the list includes computed maps (one of the first, crude computed maps was that of Eric Knudsen in the catfish electrosensory midbrain, before he went on to show the elegant acoustic one in the owl; Peter Hartline's rattlesnake infrared map in the tectum was another), parallel pathways for submodalities, several ways for dealing with unwanted reafference, central filtering, best frequencies for amplitude modulation, descending control of adaptation rate in medullary nuclei, and several other principles that may apply to other modalities.

The auditory modality is considered to be part of the octavo-lateralis system in aquatic vertebrates and may actually involve electroreception! Hal Davis and others have suggested that the cochlear microphonic is a step in the transduction of sound. I had a hobby for years of asking cochleologists how big the cochlear microphonic is right at the hair cell. Answers scattered widely, and I had to remind myself that science does not normally work like a parliament or a bookie joint in arriving at decisions.

I got further into auditory research through diplomatic channels. My old friend Yasuji Katsuki and I had just co-organized a satisfying symposium in Tokyo, supported by the U.S.–Japan Bi-National Science Program, and we realized that a study of the unique performance of dolphins in echolocation would be an appropriate follow-up, hands-on research collaboration between our countries. My associates Nobuo Suga and Allan Grinnell were experienced auditory physiologists. Katsuki put together a team from his side, both national agencies approved, and we had two short seasons of joint experiments. We learned that two parallel auditory systems are beautifully clear and already separate at the midbrain level, one for processing social communicating sounds and the other for echo-locating sounds; we believe that similar parallel subsystems exist in other animals but are somewhat more difficult to distinguish. In the echo-locating system, frequency modulation direction and span are effective in governing amplitude of response even within a 20-μsec, average 50-kHz ultrasonic click, and the rise time of amplitude modulation is discriminated even down to 20 μsec or less. Sounds—at least the clicks—enter the head principally through the mandible rather than the external auditory meatus. Far-field auditory brainstem responses (ABRs) are particularly robust and astonishingly similar to those of the rat and other mammals, including the precise latency of each wave.

We wondered whether anything like the ABR—which is so consistent in all mammals tested, including manatees (expeditions to Brazil and Florida), that one can speak of homologous waves—could be found in birds, reptiles, amphibians, teleosts, and elasmobranchs. Jeff Corwin, Jeff Schweitzer, and I surveyed species of these groups (Corwin et al., 1982) and found something quite similar, despite the great differences in the sense organ. The ABR can be averaged from an impressive distance, unlike anything known in other modalities, has several fast waves and then slower waves, but neither can be individually homologized outside the mammals. Corwin brought an intimate knowledge of elasmobranchs and together we showed that at least some families of sharks can hear rather faint sounds from some distance away in the air—or at least the brain responds at the midbrain level (Bullock and Corwin, 1979). This study was facilitated by a period on the coral reef at Eniwetak atoll in the Marshall Islands, where we could catch baby Black Tip Reef sharks, by running them down on the shallow reef, and then suspend them with rubber bands in a small tank after placing fine wire electrodes in chosen parts of the brain. Jeff Corwin succeeded in the microsurgery to show which macula of the labyrinth is mainly responsible for acoustic reception and discovered an unprecedented range in the size of this macula between families of elasmobranchs. He also found continuous addition of sensory hair cells throughout life, more and more sense cells converging onto the fixed number of afferent nerve fibers. In the meantime other co-workers and I had studied single units or EPs to acoustic events in several taxa—insects (Suga), teleosts (Piddington, Echteler), reptiles (Campbell, Suga, Hartline), doves (Biederman-Thorson), bats (Suga, Grinnell), manatees (McClune), pinnipeds (Ridgway, Suga), and sloths.

The still poorly understood sensory system of the lateral line of many aquatic vertebrates was a logical target, which my colleagues and I took up in the mid-1980s with Horst Bleckmann. My hope was to discern the combinations of stimulus parameters the brain is interested in discriminating, which in turn might explain the marked peripheral specializations among species by finding the parameter combinations with the greatest dynamic range of response, especially in higher central evoked and unit responses. We compared species with ordinary and quite specialized lateral lines but did not hit on the "Open Sesame" that I expected. Later, Horst and his students found central units that prefer movement, and I still bet on units that discriminate texture of turbulence and distance of disturbance. Preliminary findings of W. Plassmann that there are best frequencies of amplitude modulation and that they change with carrier frequency also intrigued me. A pleasant surprise was the prediction and confirmation by Ulli Budelmann and Horst Bleckmann that a lateral line analog exists in the head "lines" of the cuttlefish, *Sepia*. Glenn Northcutt and I expected to find some sensory functions by recording from the tiny nervus terminalis in the shark, *Squalus*, but instead we found it has tonically active efferent impulses, subject to suppression by somatosensory stimulation of the face.

Sensory functions of the cerebellum in rays, catfish, gymnotiform electric fish, and rats have forced themselves on our attention in several studies with R.A. Bombardieri and A.S. Feng, L. Crispino, S.-L. Tong, L. Lee, E. Fiebig, and J. New. To mention just a few points, we are curious about the meaning of segregation of cerebellar cortical areas responsive to visual, tactile, electroreceptive, vestibular, and lateral line input in fishes; the apparently unsystematic body maps; the enormous differences in size and foliation of the cerebellum among families of rays and among families of sharks, as well as among teleosts; the prominent responses in the cerebellum to stimuli applied to certain parts of the cerebral pallium; and the specific enhancement or suppression of sensory EPs in the tectum or pallium by properly timed stimuli to the cerebellum.

EEG and EP/ERP Compound Field Potential Thread

In a preliminary survey of several phyla in 1945, stimulated by the early work of C.L. Prosser, I noted that the ongoing activity of the higher ganglia of all the invertebrates examined—insects, *Limulus*, crayfish, slugs, and earthworms—was alike in being dominated by single unit spikes, with weak and inconspicuous slow waves. However, such activity of all the vertebrates examined—fish, frogs, rats, and monkeys—resembled human brain waves in being dominated by slow waves with rare or inconspicuous unit spikes. This double-sided puzzle (why are spikes so readily recorded in invertebrates but demand special technics in the vertebrates, and why are slow waves the opposite?) is important at two levels: what is the biophysical explanation, and what can be the behavioral or organizational meaning, whether consequence or cause?

The puzzles remain unsolved, although a few possible insights may be relevant. After looking at compound field potentials in many species, places, and conditions, I am betting (call them working hypotheses) that the slow-potential side of the puzzle has a basis in subthreshold synchronization and consequences in cognitive style, and that the spike side of the puzzle has bases partly in tissue impedance, partly in cell size, and possibly in the extent of glial membranes. Each of these variables cries out for quantitative natural history.

The similarity of the EEG among vertebrates, from fish to mammal, at least in the shape of the power spectrum, is even more intriguing because the structure of the cerebrum, especially its mantle, is so different and the functions and organizational dynamics are probably equally different. My hypothesis is that differences in electrophysiological dynamics exist, although they are overlooked in the preoccupation of the literature with the voltage-vs-time plot and the Fourier spectra. Hence my expert colleagues and I have been searching for new or unfamiliar descriptors of more cooperative properties on finer scales that might reveal a difference among taxa, or among brain states, stages, or parts. I believe that these compound field potentials are information-rich in ways we have not learned how to assess.

We began with coherence (a frequency-specific measure of cooperativity between two simultaneous time series), especially its distribution and spatial fine structure, in the millimeter domain. Later we examined the temporal fluctuations in the fraction-of-a-second domain. Recently we took the first extensive look at the bicoherence on similar scales; this measures a nonlinear higher moment, the quadratic phase coupling between frequency components. Again we find very local differentiation and short-term shifts. Both approaches show that essential dynamics of the EEG are not fundamentally global or large in scale but extremely local and never steady for more than a second or two but fluctuating in a way suggestive of complex, local processes, mainly nonrhythmic. The structure of activity and its origins are apparently quite different from the generally accepted view, which is based chiefly on scalp recordings and analysis that assumes sinusoidal oscillators and independence of frequencies. These conclusions have not yet resonated with many authorities and have the status of fringiform perpetrations.

This last statement summarizes the status of these ideas among cognoscenti who appreciate compound, slow waves. But a large segment of those investigating central processing do not find such waves worth discussing, let alone recording, and confine their data to the spike firing of units. A regrettable degree of mutual disparagement between those who favor the single-unit spike approach and those who favor the compound slow-potential approach has held back progress. Having done a good deal of each, it is my position that we need both windows, that they are not redundant but reveal distinct fractions of the whole—and together far less than the whole.

I am still in the stage of groping for descriptors that might measure other cooperative properties of the complex vector sum of large numbers of generators and slow as well as fast processes that we believe constitute the EEG as well as the EPs and the event-related potentials (ERPs). My bet, that the time series we record is information-rich, includes the large, seemingly stochastic component. This component should not be called noise (antisignal, in dictionaries), and neither should a large or substantial amount of noise be assumed to be present in every nerve cell; we know better.

The raw record and its decomposition into linear spectra of power, coherence, and phase at each frequency are quite inadequate as descriptors and in my opinion have misled many workers into accepting that the vertebrate EEG is basically a mixture of rhythms from more or less independent oscillators. Even with the limited view of these linear methods, we found abundant evidence, over more than two octaves, that the frequency components isolated artificially by the Fourier transform are not independent but tend to covary in space and time as though the generators are not oscillatory but wide-band events—in the general case. Of course, it is well known that under special conditions one or two, rarely three rhythms, can stand out sufficiently from the wide-band background (for example, alpha, theta, and gamma rhythms and their subspecies) to justify the inference of oscillators. These conditions account for only part of the time, leaving most of the lifetime of most mammals, and especially the nonmammalian majority of vertebrates, without evidence of rhythms.

Nevertheless, while recognizing that the prevailing state, without evidence of rhythms, includes alert, attending, and cognitively active times, I am fascinated by the special conditions that induce rhythms of a wide variety, from those of jellyfish, sensory receptors, and denervated muscles to those in higher brain levels after onset and offset of certain stimuli, those accompanying apparent expectation and presumed cognitive processing, such as "binding." We are in a very early stage of understanding their mechanisms and their functional meanings.

The phenomenology of brain activity is still little known with respect to the second-by-second time course and the millimeter-by-millimeter spatial distribution of activity, particularly signs of interactions, synchronization, cross-correlation, or other forms of cooperativity. It is rare to find such detailed studies as Walter Freeman's, with many closely spaced recording electrodes, analyzed with fraction-of-a-second temporal resolution. We badly need a lucky guess whether the most insightful measure will be coherence and its derivatives, partial and multiple coherence, or the nonlinear higher moments of quadratic phase coupling in the bispectrum and bicoherence, or estimates of mutual information or entropy, or dynamical forms of dimensionality and attractors—or something else! The issue of scale has a serious effect. Coherence between pairs of loci falls off to insignificance in millimeters, on the average, both subdurally and with gross electrodes in the depths of the temporal lobe in rats and rabbits (hardly twice as far in humans) but often spreads much less when recorded with microelectrodes intracortically. Recorded on the scalp, it sometimes spreads much farther. It's a jungle in there—a fascinating community of diverse species and interrelations—and, according to my intuition, the greatest reservoir of new principles yet to be discovered.

The EPs—a term I use in an old-fashioned sense for the relatively more exogenous, lower-level responses, time-locked to sensory stimuli with little or no cognitive dependency—were a major aim of several projects cited in the section, Sensory Physiology Thread. They come into play when a sensory event stirs up either new activity or "reordered" (phase shifted) ongoing activity, or both. Commonly, the EP is a complex sequence of responses; a simple event such as a flash of light or an acoustic click triggers a succession of faster and slower central processes, and often induces a number of cycles of an oscillation at a characteristic frequency (Bullock, 1992). EPs are useful for proving sensitivity to a stimulus, showing specialization compared to other taxa, tracing pathways, showing alteration in the dynamical properties at successive stages of processing, and interactions with other modalities.

Sharing many of the puzzles of the EEG are the ERPs, a term I reserve for relatively more endogenous, higher-level responses, time-locked to events that in humans would have a large cognitive component. Bob Galambos and his students had been pulling discoveries out of the hat for years before it finally sank in to me that we knew nothing of the evolution in nonmammals concerning the kinds of "cognitive waves" they were studying in humans, time-locked to a thought ("There's one!" "What's that?"). We began with fish and the paradigm of the omitted stimulus in a regular train of stimuli. It quickly developed that rays and grunion (teleosts) and also turtles show large, clear, and complex sequences of waves to missing stimuli; we call them omitted stimulus potentials, or OSPs. A few repetitions of a simple stimulus in a certain range of interstimulus intervals may reveal a decline in the EP and, if the train stops or a single stimulus is omitted, a relatively large rebound complex, with fast, slow, and oscillatory phases—the OSP. The diminished EP may be viewed as a suppression of the OSP that would have arisen if the stimulus were not there; the OSP is a postinhibitory release. Its nearly constant latency after the due-time of the missing stimulus reflects a kind of expectation of something exactly on schedule. We found an OSP already in the retina for flashes, and in the first brainstem nucleus for some other modalities—telling us that it need not be a higher cognitive process but an early and relatively simple consequence of the simultaneous excitation and inhibition from each stimulus, with asymmetrical time constants of buildup and decay. The higher brain levels may add further meaning and dependence on the form of attention involved. We believe it may be relevant to investigators of human scalp waves under subtle cognitive regimes that there may be major precognitive processing that determines some of the dynamics. Because we do not know where gnosis comes in, these waves and the regimes invented for research on humans, to the extent that they can be adapted for other species, might be a powerful tool for uncovering hints about the evolution of cognition. My strong bias to much of the literature on the origin of consciousness and intelligence is that, as a zoologist, I expect them to come in degrees—not along a single, smooth incline but with saltations and qualitatively different varieties and components. Most importantly, I like to underline that they are not too slippery or vague to investigate and that a major agenda of great interest and challenge to ingenuity is still ahead (Bullock, 1986b).

Evolutionary and Comparative Thread

These considerations lead me to an even wider proposition, a deep-seated belief that, for basically complex questions such as the operations of the brain, comparing taxa can contribute a unique perspective. A long list of examples is already known (Bullock, 1984a), and I am sure even more fundamental quiet revolutions are coming. A conclusion I defended in an essay in *Trends in Neuroscience* (1986a) is that differences found between taxa are as important as commonalities, in understanding how brains work and how life should be understood.

Nature has provided two great gifts: life and then diversity of living things, jellyfish and humans, worms and crocodiles. I don't undervalue the investigation of commonalities but can't avoid the conclusion that diversity has been relatively neglected, especially as concerns the brain.

My penchant for comparison and fascination with differences between taxa (as well as between individuals, life stages, and states, though these three never found much time in the agenda) surely dates from the beginnings of my biological exposure to diversity—sea shells, invertebrate phyla, coelenterates, and polychaetes. My teaching, besides Zoology 1A, was largely comparative—physiology, invertebrate biology, and neurology. Whereas a lovely literature on "comparative" neurobiology brings out a long list of intriguing stories, it does not automatically lead to comparative principles. Most of it is general physiology on favorable species. Some is the study of adaptations to certain environments or lifestyles—lateral radiation or microevolution.

An explicit interest in macroevolution and in differences between taxa at the level of classes and phyla, whether or not they can be explained as adaptive, dates from graduate student days when I was much impressed by the arguments of Richard Goldschmidt and thought that they were not getting the acceptance they deserved. But it did not appear in my own writings until the historic pair of symposia mounted by G.G. Simpson and Ann Roe on evolution and behavior in 1955 and 1958 (Bullock, 1958b).

Another long period elapsed before my colleagues and I did something further, namely examine many taxa, put together a list of species—mostly fish—that have or that lack a specialized peripheral and central electrosensory system, and then propose a phylogeny for this trait (Bullock et al., 1983). Probably less read than this—or another study, with Jean Moore and Doug Fields on the evolution of myelin—was an editorial of potentially broad significance in the newsletter of the International Brain Research Organization on "The application of scientific evidence to the issues of the use of animals in research: the evolutionary dimension in the problem of animal awareness" (Bullock, 1984b).

Elsewhere (see sections A Technical and Mathematical Leitmotif, and EEG and EP/ERP Compound Field Potential Thread), I have told the story of my early and long drawn-out interest in the evolution of that sign of activity in organized nervous tissue, the compound field potentials such as "brain waves," and evoked and ERPs—an interest that is still far from satisfied because some basic answers elude us, largely from inadequate study of nonmammalian and invertebrate groups with modern methods.

Most recently, I have been beating the drum for more explicit study of the differences between brains of different classes and phyla that are obviously distinct in the level of complexity of the brain (Bullock, 1993b). Complexity is defined as the number of kinds of parts, processes, interactions, and behavioral consequences in repertoire and discriminations. First we have to distinguish between "lateral" radiations as adaptive changes within approximately the same general grade of complexity and "vertical" changes in grade, which may or may not be obviously adaptive. Then we can focus attention on the latter. Low-power microscopic anatomy indicates conspicuously more complex histological differentiation in some orders of polychaete worms than others, and the same for some arthropods, for some molluscs, and for "higher" compared to "lower" vertebrates. Yet it is astonishing how meager our information is about the detailed basis of complexity, particularly in physiological processes and interactions but also in behavioral abilities, knowledge, discriminations, and shades of response. Because evolution is a central feature of the biological world and nothing else approaches the span of complexity that the nervous system has evolved, I conclude that we have neglected a major facet of the biological world, presumably in our preoccupation with commonalities and adaptions within a grade of organization.

Behavioral Thread

I could not teach a course in animal behavior without a lot of preparation. It took me a long time to understand what some authors meant by "ethology," although I was privileged to be a member of the historic 1954 symposium convened by Bill Verplanck, when several European ethologists made their first full-fledged explanation this side of the Atlantic, in the basement of Harvard's Memorial Hall. My guess is that I was invited, not because of a known competence in animal behavior, but because of the appearance of a single paper in 1953, quite out of my usual turf, on predator recognition by gastropods—an ability then almost unknown in invertebrates, except for scallops and a few other species. That study had started in 1947 when I was teaching field invertebrate zoology for the University of California, Berkeley at the Hopkins Marine Station, under Ralph Smith and Frank Pitelka. On the last day, students gave reports and Eugene Haderlie, studying the movements of limpets, described low tide species that fled from contact with a few tube feet of a starfish arm. That was something new, but he did not elect to continue and collect convincing evidence, so I did, over several years, and the 1953 paper resulted.

Intact, behaving animals were a common denominator of my papers—jellyfish, earthworms, sloths, sharks, cuttlefish, and others. Some studies used restrained subjects or "preparations" with stimuli and experimental questions relevant to the natural conditions. Where and how does patterned discharge arise (Bullock, 1961a)? Can recognition of complex, natural combinations of stimulus features (for example, small, dark, sharp-edged, moving contours within a 5° visual field) occur early in the visual pathway, as claimed by Lettvin, Maturana, and co-workers (Grüsser-Cornehls et al., 1963)? What do electric fish do to minimize the jamming effect of neighbors discharging at nearly the same rate (Scheich et al., 1973)?

Some of the behaviorally slanted questions precipitated reviewish essays, for example on animal minds, on startle responses, on suggestions for an agenda on comparative cognition (Bullock, 1986b), and on the comparative neurobiology of expectation (Bullock et al., 1993b; see also EEG and EP/ERP Compound Field Potential Thread).

The three-toed sloth is a special case. Watching this species and handling it in the American tropics, the notion was irresistible that such an elementary feature of its whole behavior and habit of life as slowness ought to be amenable to physiological study. At least we should be able to exclude one of two alternatives in the lovable and tractable three-toed genus, which is much slower than the more familiar two-toed form. Is it (1) capable of quick movements, like a lazy cat, if induced or motivated properly, or (2) is there a lower-level bottleneck, perhaps in the muscles, preventing quick movements, even if the brain commands them? Per Enger and I were able to answer this, virtually excluding the first and definitely confirming the second alternative (Enger and Bullock, 1965). Subsequent work convinced me that the brain is not issuing commands that the muscles cannot execute. The sloth brain is slow in conduction, in transmission, in EPs, in rhythms such as nystagmus, and in other measures—but I am sure the major specialization for slowness still eludes us. A leading clinical neurologist, James Toole, wondered if this animal is a model of a clinical condition called myotonia and came to our lab to do a long series of tests. That was one of the most satisfying collaborations I have had with clinicians. Toole was able to exclude his hypothesis as well as some others such as hypothyroidism. My hunch is that the specialization is diffuse and multiple—perhaps a combination, for example, of neurons that cannot accelerate their firing rate rapidly, plus perhaps some transmitter or modulator equilibrium in limbic centers way over to one side of the mammalian norm (Bullock, 1983). This is clearly an unfinished agenda item—still interesting, heuristic, and potentially basic.

Unfinished Projects

The story just cited is not my only unfinished project, and my history would be distorted if it lacked reference to the many worthy but over-ambitious, dumb but fun, and half-baked projects that never saw the light of day or the lamp of publication.

The one with the greatest longevity is a taxonomic monograph of the eastern Pacific enteropneusts, a task I inherited in 1939 from W.E. Ritter, founder of SIO. His manuscript of ca. 1898 on a passel of new species from southern California to the Aleutian Islands—the specimens and slides of which had dried up and faded beyond recognition—plus another gaggle of new species that turned up during and after my thesis work, together would add a substantial percentage to the known world list. A Byzantine series of twists and turns has so far failed to allow the combined manuscript to be completed, illustrated, and published, although in its ups and downs it has been within 5 percent of completion. Fortunately, there is still hope, even though two of the coauthors are deceased.

Less dramatic were various aborted studies such as those on the physiology of bryozoan and nemertean nerve nets, and on oscillatory, visual, induced rhythms in the brains of 17-year cicadas, like those reported by Jahn and Crescitelli (1938) in grasshoppers and moths. I allow myself the embarrassment of touching on these few examples from a much larger set lest an inexperienced reader get a false impression of efficiency or catch per unit effort!

Unfinished, too, are various projects under the rubric of hobbies. A fair number of bonsai are still taking final shape on our patio. A small number of free-form sculptures in clay, wood, and stone are always vulnerable to another reshaping. Both of these responsive metiers have given a degree of personal satisfaction while challenging the imagination and creative juices.

From the vantage point of experience, I ought to have some advice for young scientists from my mistakes—and I have. By all means, keep a day book of some sort—not necessarily a full diary but one with entries that record when you did something of interest and whom you met, especially on trips. Identify your research with some big question, on every possible occasion. Don't wait until all the data you think you need have come in before analyzing, at least enough to decide what the story is. Don't print out even a few sample plots to test your plotting program, unless you label them with every relevant parameter; assume they will be kept, will get into the wrong folder, and, if unlabelled, will puzzle the stuffing out of you. Don't exaggerate, even in conversation, except when telling jokes. Here I stop, before the negative slope of wisdom becomes a cliff.

La Jolla, Medicine, and Marine Biology, R/V *Alpha Helix*, NRP, SFN, IBRO, and ISN

I don't know just why we moved to La Jolla; I was happy at UCLA, associated with the Department of Biology and the Brain Research Institute. The prospect of being a bridge between marine biology and medicine, of helping my old UCLA friend Bob Livingston realize his dream of creating the first Department of Neurosciences, and the unconventional plan of the medical school were all appealing. The so-called Bonner plan, now officially abandoned, actually accomplished a great deal, though not all of its promise. The plan provided that every department of the medical school had clinical responsibilities and most departments had nonclinical faculty. Many faculty positions budgeted in the medical school were farmed out to nonmedical departments and those departments participated in the preclinical teaching. Core courses were controlled by committees, not departments, and there were no departments of anatomy, physiology, or biochemistry.

The curriculum was not quite so unusual but provided free time for elective courses and a required thesis or creative project to give each student the experience of investigation. The boundary between the medical school and the rest of the campus was appreciably fuzzier than elsewhere. All these features were positive, and I enjoyed being the first chairman of the electives committee and spending time on self-paced learning resources, tutorial sessions, and optional exams. Many meetings and beautifully uninhibited planning went into designing the Ph.D. programs in neurosciences and in physiology-pharmacology, writing training grants, formalizing a program in marine biomedicine, and recruiting faculty, as well as into committees on the design of new buildings, on privilege and tenure, university-wide coordination, and others.

Locally, we maintained for years the Marine Neurobiology Facility (MNF), a joint operation of the UCLA BRI and UCSD SIO, in the third floor of a new building, called the Physiological Research Laboratory, built from joint NSF grants to Per Scholander for SIO and J.D. French for the BRI. The same grants also covered large outdoor pools and the R/V *Alpha Helix.* The first chairman of the MNF was Susumu Hagiwara, who was recruited in 1965 as the first neuroscientist at UCSD; he had been a postdoc in my laboratory at UCLA and gradually developed his own space, grants, and group. He brought a large and brilliant group to La Jolla and spent four productive years there. After he was lured back to UCLA in 1969, I managed the MNF as a group of laboratories for visiting scientists from UCLA and elsewhere, plus the larger entity, called the Neurobiology Unit of SIO (officially an "Affinity Group"), which included the MNF, plus my own laboratory and eventually those of Walter Heiligenberg, Jim Enright, Adrianus Kalmijn, and Glenn Northcutt.

SIO is a stimulating place and it keeps one's perspective not only global but cosmic. Despite an omnipresent, fortunately minority view that only those working on blue water oceanic problems belong, a large faculty of broad and deep thinkers could be encountered in the corridors or the lunch line at Snackropolis on Bikini Plaza. I will mention just a few whom I saw frequently: P.F. Scholander and J.D. Isaacs (both of whom left stimulating memoirs), A.A. Benson, G. Arrhenius, W. Munk, W.A. Nierenberg, F. Azam, and E.D. Goldberg.

The R/V *Alpha Helix* was near completion in the shipyard when I was invited to join the National Advisory Board for the Physiological Research Laboratory, which included its shore facilities and the ship, all regarded by UCSD and NSF as national facilities. Under the chairmanship of A. Baird Hastings, this board solicited and evaluated proposals for comparative physiology and biochemistry that justified the trip, exotic locations, and floating platform. Each selected proposal became a one- to three-month program—a segment of an expedition of 12 to 18 months. The principal investigator or proposer became the chief scientist of that segment and chose about 10 colleagues from anywhere in the world, including students and senior scientists, all concentrating on projects in the same broad field—normally 15 or 20 projects with different combinations of coworkers. Joining the vessel and each other in some remote port, these people experienced a magical process by which new projects sprang up, in addition to those that had been well prepared.

The ship operated in this mode, as Scholander had envisioned and described in his original application for funds, for about five years, completing some 30 programs, involving more than 300 scientists. I was chairman of the National Advisory Board for several of those years and chief scientist for two programs in neuroethology, one on the Great Barrier Reef and one on the Rio Negro, the fifth tributary of the Amazon. This innovative and successful concept of Scholander's could not, however, be maintained at this rate, for lack of high-quality proposals. Having skimmed the cream, it became harder to find nonoceanographic, nonecological proposals high in merit and also in justification for both the remote location and the floating platform, because these depend on biochemists and physiologists, most of whom have ongoing programs at home and have never thought about working on exotic species unavailable at home or even at existing shore laboratories. At SIO's initiative, the vessel was transferred to and is still operated by the University of Alaska, in quite another mode.

The times were ripe in the late 1960s for the field that came to be called neuroscience. Crossing disciplinary lines began with anatomy and physiology—H.W. Magoun and many colleagues had been doing physiology in anatomy departments, notably UCLA. Some psychologists had started what grew into a mass movement into neurophysiology. The International Brain Research Organization (IBRO) had been dreamed up by a small multinational group at a meeting in Moscow and was eventually chartered in Canada in 1958. Francis O. Schmitt's Neuroscience Research Program (NRP) at the Massachusetts Institute of Technology (MIT) had put the word neuroscience on the map and explicitly included all the disciplines dealing with nervous systems. He had staged a carefully orchestrated symposium at a National Academy of Science meeting in 1967. The first of the mammoth NRP Intensive Study Programs ranging over the whole field, was held in Boulder, Colorado for a month in midsummer 1966, involving several hundred people and producing a weighty and influential tome, the first of four.

The National Research Council set up a Brain Science Committee (BSC), partly to provide U.S. representation on the IBRO Central Council and partly to think up what needed to be done for brain science, procedurally as well as substantively. At the instigation of Ralph Gerard, the committee took steps to create the Society for Neuroscience (SFN), which convened its first meeting in Washington, D.C. in 1970. I was involved in most of these events, from the recruitment of Magoun to UCLA, to the NRP, ISP, and BSC. Later I joined the IBRO Council and headed its Visiting Lecture Team Program and Workshop Program, which had significant budgets from UNESCO. By the time I became president of SFN in 1973 to 1974, it was a smoothly running operation under a superb executive secretary, Marjorie Wilson, but was financially vulnerable. Among our campaigns was one to persuade the neurochemists, anatomists, and clinical neurologists that they were wanted, another to elect Canadian and Mexican members to solidify the status of SFN as regional and multinational. We then helped local chapters to form in those countries and in many cities in the United States. With this background, it is understandable that I felt truly honored when SFN awarded the Gerard Prize jointly to my long-time friend and coworker, Susumu Hagiwara, and me in 1984. I had known and admired Ralph Gerard through many of his phases—in Chicago, Ann Arbor, and Irvine—and knew his personal role in the founding of the society.

One other organizational caper may be of interest. In 1981 J.-P. Ewert of Kassel, Germany, invited a large number of worthies to a NATO-sponsored symposium on recent advances in vertebrate neuroethology, and staged a memorable meeting. Near the end, some of us saw the opportunity and asked for a business meeting to think about the future. Probably the rank and file thought there would be polite thank-yous and a suggestion that we meet again in a few years. By prearrangement, however, a few plotters had a preamble and a motion ready to propose setting up a steering committee to create a permanent, new society, to be called the International Society for Neuroethology (ISN). We had to do some quick-stepping to prevent its being dedicated to vertebrate animals. An organizing committee under Masakazu Konishi was authorized to assemble a list of invitees to charter membership and to conduct an election. Eventually I was elected the first president (1984–87), by a statistically insignificant majority. I was saved from presiding over a stillbirth by the magnificent response of Kiyoshi Aoki of Sophia University in Tokyo and his many colleagues in Japan, who raised money and organized the first congress in 1986. ISN has weathered not so much storms as calms, and just held its fourth congress.

Meetings, Lectures, Intussuscepting, Pontificating, and Globe-trotting

It suffices to say but little about the many trips taken to regular and to irregular meetings and to give lectures, colloquia, or seminars. The meetings, both the giant and the cozy, are major pauses along the way. The regular ones, like milestones, permit periodic reports of your progress; the sporadic symposia, conferences, and workshops allow extended presentations and discussion with fellow specialists. Both types bring old and new friends and, increasingly in the last few decades, overseas colleagues. A feature of science that we tend to take for granted but should appreciate as different from most other walks of life is the instant friendship and ease of meeting people from other countries and cultures. Side trips to visit laboratories and give lectures double the value, both scientifically and personally. I have a long list of hosts and hostesses I should like to acknowledge for an even longer list of first experiences in interesting venues.

In a category by itself belong the meetings of the NRP: "stated meetings," "work sessions," and ISPs. This instrumentality of MIT, created and operated by Francis Schmitt was a highly successful experiment in scientific communication. A core group of diverse people willing to come together several times a year to think about the nervous system included mathematicians, physicists, anatomists, psychologists, chemists, physiologists, and others, from half a dozen countries. Four to six meetings a year were held on special topics and a dozen or more world experts were invited to each, producing a Work Session Bulletin on the status of the topic. I was privileged to be an early (1962) member and went to three or four meetings a year for 16 years. These were rich privileges in substance and in learning how difficult serious interdisciplinary dialogue can be and how shaggy dog stories can help.

Working for national and international organizations can add up to a lot of trips—planning, evaluating, and advising—which are usually interesting and often constructive. One makes splendid friends and pays some dues for all the beneficence one owes to others. Besides the lofty angles suitable for reports, there are the memories—like shopping for saffron in the bazaar in Kuwait with Sir John Eccles, trailing his eager and quality-conscious wife, while David Ottoson and I deploy as bodyguards.

Invited lectures have meant another wide range of experiences. Some are intimidating occasions for trying out a brainchild on a hypercritical audience; others are inspiring visits to liberal arts colleges. Altogether they have formed a major part of my teaching and, from spirited feedback, a substantial source of broadening my own research and thinking. With or without honored names attached (the Jacques Loeb, George Bishop, Ralph Gerard, Alexander Forbes, Robert Dow, Clinton Woolsey, Albert Grass, Arturo Rosenblueth Lectures, and others), they are also gratifying honors that I have appreciated greatly. Being constitutionally unable to give the same lecture more than a few times, I have trod where angels fear to, over a range of topics: evolution of the brain, reliability of neurons, redundancy and equivalence classes of nerve cells, animal rights, aspects of recent history in neuroscience, integrative mechanisms, recognition by neurons, electroreception, and others.

Some of these subjects have grown into books. The 1965 treatise with Adrian Horridge on *Structure and Function in the Nervous Systems of Invertebrates* summarized about 10 kilореferences before the age of many modulators, transmitters, and channels. This work even missed by a few years the recognition of many identifiable cells in insects, crustaceans, opisthobranchs, leeches, and other taxa. Despite its being out of date, our sentimental investment in this two-volume work was severely rocked when it went out of print, without our knowledge, in a warehouse cleaning that destroyed a good many sets before we had a chance to purchase them! One feels impelled to a slightly mutated dictum: caveat auctor. Skipping over a textbook and a multiauthored monograph on electroreception, I will mention only the 1993 book, titled *How Do Brains Work?* Without pretending to answer the question globally, I had a lot of fun talking about major aspects of it, updating old essays, placing bets and picking a selection of reprints—the publisher's raison d'être for the volume.

Today the driving motivation continues: what's going on; how does it work; what's the principle of the thing; there must be a good idea waiting to be recognized—think! At this writing I am surrounded by plots of human, turtle, and ray EEGs analyzed for higher moments of nonlinear interactions among frequency components, called bicoherence, a hitherto almost untried descriptor of different states, brain parts, and species. I am nearing the end of a labor of love, keeping the Walter Heiligenberg laboratory open and active for nearly three years after his tragic death in a plane crash. My wife Martha and I enjoy our children, grandchildren, friends, church, walk-in aviary, and bonsai. We appreciate every day as a gift.

Selected Publications

Bullock TH. Neuromuscular facilitation in scyphomedusae. *J Cell Comp Physiol* 1943;22:251–272.

Bullock TH. A preparation for the physiological study of the unit synapse. *Nature* 1946;158:555–556.

Bullock TH. Predator recognition and escape responses of some intertidal gastropods in presence of starfish. *Behaviour* 1953;5:130–140.

Rao KP, Bullock TH. Q_{10} as a function of size and habitat temperature in poikilotherms. *Am Nat* 1954;88:33–44.

Bullock TH. Compensation for temperature in the metabolism and activity of poikilotherms. *Biol Rev* 1955;30:311–341.

Bullock TH, Diecke FPJ. Properties of an infra-red receptor. *J Physiol* 1956;134:47–87.

Bullock TH, Hagiwara S. Intracellular recording from the giant synapse of the squid. *J Gen Physiol* 1957;40:565–577.

Bullock TH, Terzuolo CA. Diverse forms of activity in the somata of spontaneous and integrating ganglion cells. *J Physiol* 1957;138:341–364.

Bullock TH. Homeostatic mechanisms in marine organisms. In: Buzzati-Traverso AA, ed. *Perspectives in marine biology.* Berkeley: University of California Press, 1958a;199–210.

Bullock TH. Evolution of neurophysiological mechanisms. In: Simpson GG, Roe A, eds. *Behavior and evolution.* New Haven, CT: Yale University Press, 1958b;165–177.

Bullock TH. Neuron doctrine and electrophysiology. *Science* 1959;129:997–1002.

Watanabe A, Bullock TH. Modulation of activity of one neuron by subthreshold slow potentials in another in lobster cardiac ganglion. *J Gen Physiol* 1960;43:1031–1045.

Bullock TH. The origins of patterned nervous discharge. *Behaviour* 1961a;17:48–59.

Bullock TH. The problem of recognition in an analyzer made of neurons. In: Rosenblith, WA, ed. *Sensory communication.* Cambridge: Technology Press, 1961b;717–724.

Bullock TH, Hagiwara S, Kusano K, Negishi K. Evidence for a category of electroreceptors in the lateral line of gymnotid fishes. *Science* 1961; 134:1426–1427.

Grüsser-Cornehls U, Grüsser O-J, Bullock TH. Unit responses in the frog's tectum to moving and nonmoving visual stimuli. *Science* 1963;141:820–822.

Bullock TH, Horridge GA. Structure and function in the nervous systems of invertebrates, 2 Vols. San Francisco: WH Freeman, 1965.

Enger PS, Bullock TH. Physiological basis of slothfulness in the sloth. *Hvalradets Skrifter* (Scientific results of marine biological research). 1965;48:143–160.

Bullock TH, with Quarton CG. Simple systems for the study of learning mechanisms. *Neurosci Res Program Bull* 1966;4:105–233.

Fehmi LG, Bullock TH. Discrimination among temporal patterns of stimulation in a computer model of a coelenterate nerve net. *Kybernetik* 1967;3:240–249.

Perkel DH, Bullock TH. Neural coding. *Neurosci Res Program Bull* 1968; 6:221–348.

Bullock TH. The reliability of neurons. *J Gen Physiol* 1970;55:565–584.

Bullock TH, Ridgway SH. Evoked potentials in the central auditory system of alert porpoises to their own and artificial sounds. *J Neurobiol* 1972;3:79–99.

Scheich H, Bullock TH, Hamstra RH Jr. Coding properties of two classes of afferent nerve fibers: high-frequency electroreceptors in the electric fish, *Eigenmannia. J Neurophysiol* 1973;36:39–60.

Bullock TH. Recognition of Complex Acoustic Signals. Dahlem Workshop. Life Sciences Research Report 5. Dahlem, Germany: Dahlem Konferenzen, 1977.

Bullock TH, Orkand R, Grinnell AD. Introduction to nervous systems. San Francisco: WH Freeman, 1977.

Bullock TH, Corwin JT. Acoustic evoked activity in the brain in sharks. *J Comp Physiol* 1979;129:223–234.

Bullock TH. Reassessment of neural connectivity and its specification. In: HM Pinsker, WD Willis Jr, eds. *Information processing in the nervous system.* New York: Raven Press, 1980;199–220.

Corwin JT, Bullock TH, Schweitzer J. Auditory brainstem response in five vertebrate classes. *Electroencephalogr Clin Neurophysiol* 1982;54:629–641.

Bullock TH. Neuroethological role of dynamic traits of excitable cells: a proposal for the physiological basis of slothfulness in the sloth. In: Grinnell AD, Moody WJ Jr, eds. *The Physiology of Excitable Cells.* New York: Alan R Liss, 1983;587–596.

Bullock TH, Bodznick DA, Northcutt RG. The phylogenetic distribution of electroreception: evidence for convergent evolution of a primitive vertebrate sense modality. *Brain Res Rev* 1983;6:25–46.

Bullock TH. Comparative neuroscience holds promise for quiet revolutions. *Science* 1984a;225:473–477.

Bullock TH. The application of scientific evidence to the issues of use of animals in research: the evolutionary dimension in the problem of animal awareness. *IBRO News* 1984b;12:9–11.

Bullock TH. 'Simple' model systems need comparative studies: differences are as important as commonalities. *Trends Neurosci* 1986a;9:470–472.

Bullock TH. Suggestions for research on ethological and comparative cognition. In: Schusterman RJ, Thomas JA, Wood FG, eds. *Dolphin cognition and behavior: A comparative approach.* Hillsdale, NJ: Lawrence Erlbaum Associates, 1986b;207–219.

Bullock TH, Heiligenberg W. Electroreception. New York: John Wiley, 1986.

Bullock TH, Basar E. Comparison of ongoing compound field potentials in the brains of invertebrates and vertebrates. *Brain Res Rev* 1988;13:57–75.

Smith DPB, Bullock TH. Model nerve net can produce rectilinear, non-diffuse propagation as seen in the skin plexus of sea urchins. *J Theor Biol* 1990;143:14–40.

Bullock TH. Introduction to induced rhythms: a widespread, heterogeneous class of oscillations. In: Basar E, Bullock TH, eds. *Induced rhythms in the brain.* Boston: Birkhäuser, 1992;1–26.

Bullock TH. How Do Brains Work? Papers of a Neurophysiologist. Boston: Birkhäuser, 1993a.

Bullock TH. How are more complex brains different? One view and an agenda for comparative neurobiology. *Brain Behav Evol* 1993b;41:88–96.

Bullock TH, Karamürsel S, Hofmann MH. Interval-specific event related potentials to omitted stimuli in the electrosensory pathway in elasmobranchs: an elementary form of expectation. *J Comp Physiol [A]* 1993;172:501–510.

Bullock TH. Neural integration at the mesoscopic level: the advent of some ideas in the last half century. *J Hist Neurosci* 1995;4:219–235.

Additional Publications

Alexandrowicz JS. The innervation of the heart of the Crustacea. I. Decapoda. *Q J Microsc Sci* 1932;75:182–249.

Gesell R. Forces driving the respiratory act. A fundamental concept of the integration of motor activity. *Science* 1940;91:229–233.

Horridge GA. The co-ordination of the protective retraction of coral polyps. *Philos Trans R Soc Lond B Biol Sci* 1957;240:495–529.

Josephson RK, Reiss RF, Worthy RM. A simulation study of a diffuse conducting system based on coelenterate nerve nets. *J Theor Biol* 1961;1:460–487.

Jahn TL, Crescitelli F. The electrical response of the grasshopper eye under conditions of light and dark adaptation. *J Cell Comp Physiol* 1938;12:39–55.

McCulloch WS, Pitts W. A logical calculus for ideas immanent in nervous activity. *Bull Math Biophys* 1943;5:115–133.
Pantin, CFA. The nerve net of the Actinoza. I. Facilitation. *J Exp Biol* 1935; 12:119–138.
Schultz R, Berkowitz EC, Pease DC. The electron microscopy of the lamprey spinal cord. *J Morphol* 1956;98:251–274.
Wiersma CAG, Van Harreveld A. A comparative study of the double motor innervation in marine crustaceans. *J Exp Biol* 1938;15:18–31.