The History of Neuroscience in Autobiography
Volume 1
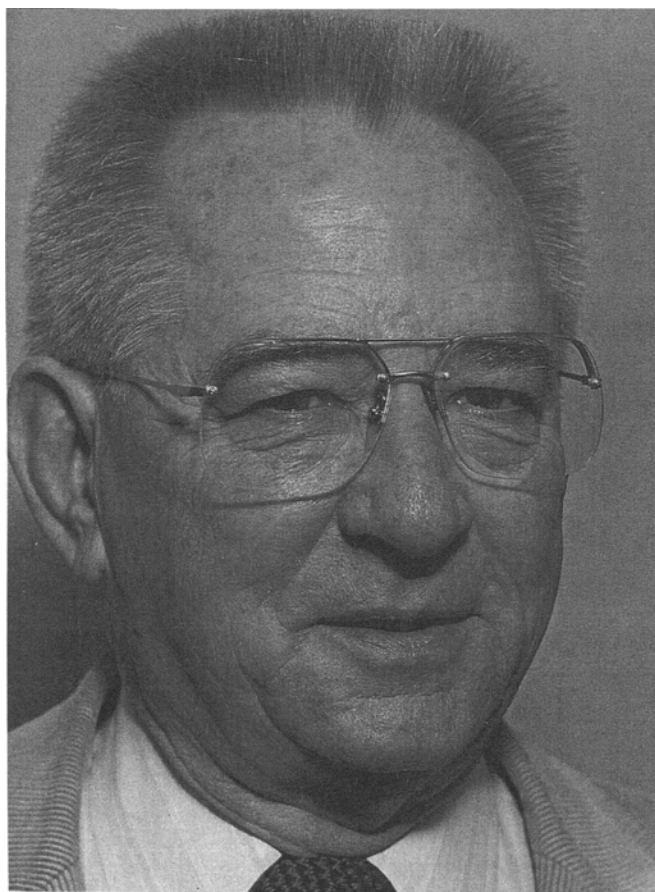
Robert Galambos

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BORN:

Lorain, Ohio
April 20, 1914

EDUCATION:

Oberlin College, B.A., 1935
Harvard University, M.A., Ph.D. (Biology, 1941)
University of Rochester, M.D., 1946

APPOINTMENTS:

Harvard Medical School (1942)
Emory University (1946)
Harvard University (1947)
Walter Reed Army Institute of Research (1951)
Yale University (1962)
University of California, San Diego (1968)
Professor of Neurosciences Emeritus, University of
California, San Diego (1981)

HONORS AND AWARDS:

American Academy of Arts and Sciences (1958)
National Academy of Sciences USA (1960)

Robert Galambos discovered, with Donald Griffin, the phenomenon of echolocation in bats. During his career he carried out fundamental physiological studies of the auditory system using microelectrodes in cats, and later studied brain waves and auditory evoked potentials in humans. He was an early and forceful protagonist for the importance of glia in the function of the nervous system.

Robert Galambos

Introduction

The subject was born in Lorain, Ohio, on April 20, 1914, not long after the vacuum tube was invented. At the age of 6, and in the first grade of a Cleveland, Ohio public school, he heard his first radio message through an earphone connected to a crystal radio receiver his older brother had built. He was about 40 years old when television sets first appeared for sale in the stores; by that time he had obtained A.B. and M.A. degrees in Zoology at Oberlin College (1936); M.A. and Ph.D. degrees in Biology at Harvard University (1941); and the M.D. degree at Rochester University (1945). Also, penicillin had been discovered, Hitler and Hirohito defeated, and a remarkable expansion of research on the brain was just getting under way throughout the world. This essay provides some details about the subject's participation in that effort.

In autobiographies this use of the third person past tense is the way writers inform readers they feel uncomfortable with the topic being discussed. My problem is that I have already published one of these self-portraits (Galambos, 1992), which is probably all the world needs. How will I cover the same old ground in a new way? The questions I asked in search of the answer may be worth preserving.

Who writes an autobiography? Among modern scientists, almost invariably, someone who has been asked. Benjamin Franklin, our first great scientist, wrote a long one, and Abraham Lincoln wrote a very short one, but we don't remember either man because of what he wrote about himself. If what you produce during your lifetime is really worthwhile others see to it the world does not forget.

Why does a person agree to write one? If you have grandchildren, which most autobiographers do, the immortality your genes clamor for is already assured. Duty? Vanity?

For whom do we write? I have yet to find someone who makes this explicit, but I will aim my autobiography at the young person about to submit a manuscript reporting his or her first successful experiment,

knowing full well that when I was at that point in my own career the bottommost item on my reading list was an account of someone's life.

What should I write about? I asked several friends, and their answers clustered around two themes. Many wanted to know how I decided what I was going to do, both as a student before committing myself to a research career, and then every morning as I opened the door of my place of business and walked inside. Students often raised practical matters, such as how to write a good scientific paper, how many mistakes are you allowed to make during a career, and so on.

I finally settled on what follows, which has three parts: my background, my work, and what I would do in the future if I had one. It is a story about people, ideas, what we accomplished together, and the environments in which we worked during the most remarkable 60 years in the history of science, so far.

Personal Matters

I was the third of four brothers. My father (1880-1954) and mother (1885-1969) came through Ellis Island from northeast Hungary around 1895 and met for the first time in Lorain about 10 years later. My paternal grandfather (1844-1907) was a peasant who died in the same farmhouse where he had raised two daughters and four sons, of whom my father was the youngest. (I have a copy of the von Galambos coat of arms and once exchanged letters with the last nobleman of the line; there is no evidence whatever our families are related.) My mother, Julia Peti (Petty), was the oldest of five siblings; her father was a schoolteacher who taught her to read and write before she was brought to America by a relative at the age of 12 or 13. It is interesting and sad that I retain nothing that I may have been told about my grandmothers.

My father said his first purchase was an English dictionary, and that he set himself the task of learning to spell, pronounce, and use three new words every day. By 1905 he had apprenticed as a carpenter and was taking a correspondence school course covering the building trades, and would soon set himself up in the house-building business he successfully conducted throughout his life. He was proud that his word and handshake were all anyone needed to close a business deal.

My mother was a small woman—perhaps five feet tall—who took nonsense from no one. She attended night school to improve her English skills, and I retain dozens of letters she wrote in a curiously antique hand. She taught her sons promptness because the early bird catches the worm, frugality because a penny saved is a penny earned, and honesty because it is the best policy—teachings many young people today never even encounter, let alone learn. As an adult I spent a day or two with her whenever possible, managing this once or twice every year at her home in

Florida. She told me during my last visit she had delayed going to the hospital because she was certain she would come out "feet first" the next time. An inoperable gastric carcinoma had finally blocked her digestive tract. My mother was much loved; three of her doctors helped carry her casket and, as she had instructed, we drank champagne during the good-bye party at my brother's house afterwards.

My parents were intelligent but not intellectuals; there were few if any family discussions about books, religion, poetry, or politics. My father did once outline for me his theory of vision; it involved particles emitted by the eye that reach targets in the environment. My mother listened proudly while I described my research results, but she still wondered how soon I was going to go to work when I was almost 40 years old.

Physical Well-Being; Financial Security, Domestic Tranquility

Prior to a mild heart attack at age 78, my most serious medical problems had been a tonsillectomy at 19, a frequently aching back, and an occasionally painful knee corrected by arthroscopic surgery at age 69. At 65 I quit smoking after 50 years, began jogging, and kept an almost daily log of distance run for the next 10 years. Its entries occasionally note what a godsend this exercise was for me physically and mentally, and they also trace, inadvertently, the order in which my genes have progressively turned off one bodily process after another. At 81 I have finally accepted the fact that a few years at most remain for completing what I still want to do, and am mildly amused at how, like so many other aging people, I stubbornly refused to accept my mortality.

Money has never been much of a problem, although I was close to 40 before repaying what I had borrowed from parents and others. Throughout my adulthood, the national economy expanded, salaries increased regularly, and inflation boosted the value of the homes I sold. As a result, I found it possible to live well with my family and to do such extra things as pay the salary of a collaborator for a month or two between grants, commute to Budapest to work with colleagues on an experiment, and assemble a collection of old pocket watches and Navajo rugs.

I have had three wives, each a strong person who meshed her career plan with my own. My first wife, now Jeannette Wright Stone, is widely known for her contributions to the field of early childhood education; after more than 30 years, she chose to divorce me for another man. The second, Carol Armstrong Schulman, a neuroscientist in her own right, left me by committing suicide during one of her bouts of depression. The third, Phyllis Johnson, joined me in 1977, and since then I have known more peace, order, comfort, and companionship than a person has any right to expect. Jeannette and I have three daughters, who, between them, have given us five grandchildren.

Awards and Prizes

My honorary degrees include the M.A. routinely awarded all Yale professors who do not already have a Yale degree and the M.D. awarded by the Swedish University of Göteborg, for which its then-rector, my friend Holger Hyden, the glia specialist, is probably responsible. I also have several meritorious performance commendations from the Army. A former colleague, George Moushegian, told me recently that during the past 20 to 30 years he has repeatedly submitted my name for various honors given specialists in hearing matters and is frustrated that none has ever been awarded. Perhaps he overestimates my qualifications, but certainly my ability to say no when offered jobs that would take me away from the laboratory has played a part. My own view is that I am often arrogant and cranky, and this turns people off.

Introduction to Research, Oberlin College, 1934-38

I first systematically encountered biological facts and concepts as a college junior in 1934 and found them surprisingly easy to grasp, remember, and manipulate. My math and physics grades were B with a sprinkling of C. I was delighted by my special knack for Biology, which in retrospect seems easy to interpret in the context of Howard Gardner's idea of multiple innate intelligences (Gardner, 1983). Undergraduates in 1935 were strongly inclined toward J.B. Watson's behaviorism, sometimes illustrated by the fantasy that a given baby can be fashioned into either a musician or a mathematician by selecting the proper stimuli to create its repertoire of reflex responses.

The conceptual distance is immense between such ideas and the current explanations, which assign a huge contribution to the genome ("nature") and whatever remains to "nurture." Gardner's Seven Intelligences account much more aptly than J.B. Watson's reflexes for the musical genius of Mozart and Bach, the mathematical genius of Turing and Leibnitz, the verbal genius of Shakespeare, and the athletic genius of ballet dancers and basketball players. It seems believable to me that each of us arrives with a unique mix of Gardner's seven, and we thereafter develop these to the extent permitted by where, and how long, we happen to live. Of course, people still take sides on the nature-nurture dichotomy, but my quaint behavioristic view disappeared forever following the publication by J. D. Watson and Crick, in 1953, of what Watson has called their "insight into the nature of life itself."

About the Scientific Paper

My first encounter with one of these took place in my junior year in the departmental library as I was preparing my first seminar report for C. G. Rogers, a professor of Comparative Physiology. The paper, by W. R. Hess,

dealt with the nervous system of the earthworm, and it ended with a complete summary of the paper's objectives and results! What a stunning surprise! How informative and helpful! I gushed on like this in my presentation.

I have never read an account of how the scientific paper, that unique creation of the scientific community, evolved to reach its modern form. The mathematician Mark Kac once called them five-part Scientific Sonatas: Summary, Introduction, Methods, Results, Discussion. It is clearly the best known way to organize a scientific message; try to invent something different and be convinced. Meanwhile, here are two tips if you need help: first, study a few published examples you admire and note how often the writers follow the rules you will find in Strunk and White's *The Elements of Style*. Second, edit ruthlessly; you can always improve what you have already written.

My First Laboratory

Raymond Herbert Stetson, professor of psychology at Oberlin College in 1935, was one of those unsung heros of American science: the small-college professor who inspires and guides its recruits at the time they are most vulnerable and educable. He introduced me to the research plan, the research lab, and the research discovery. In my two years with him (September 1935-37) I learned all the fundamentals: how to formulate the problem, plan the work, collect the apparatus, do the experiments, analyze the data, make the figures, write the paper, get it published, and, finally, how to teach what you know about all this to others. See Kelso and Munhall (1988) for biographies of this remarkable man.

Roger Sperry and I graduated together in 1935 and then did our master's degree research in Stetson's Oscillograph Laboratory, which, thanks to its chief technician, James M. Snodgrass, was about as well equipped for electrophysiological measurements as the Forbes-Davis Harvard Medical School laboratory to which I would shortly go. Stetson's lab regularly included a few senior visitors who had come to work on the mechanisms of speech production, or motor phonetics, Stetson's special field of interest. It was there that I joined the first of many such small, intimate fellowships that unite for the purpose of discovery. Members of every healthy lab bond closely together, like all comrades who seek the same goal. Years later, at Yale, I created similar temporary groups by organizing summer-long, six-days-a-week opportunities (five in all) where young people gained hands-on experience with electrophysiological instruments and developed a certain skill in using them. Still later, in San Diego, this became a three- to four-day annual symposia (seven in all) on the then-new auditory brainstem response; the attendees listened to lectures, but more importantly they carried home tracings of the responses made with their own hands. I have always wanted my own laboratory to be like Stetson's, a place where people take pleasure in creating their own experiments and discoveries in the company of others doing the same.

Don Lindsley introduced me to single units when he visited Stetson's lab in the spring of 1936. While at Harvard (1933-35), Don had inserted electrodes consisting of a fine insulated wire inside a hypodermic needle into arm and leg muscles of human subjects to isolate single motor units, which he defined as the collection of muscle fibres innervated by a single motor neuron. Stetson had heard of these measurements and asked Lindsley, who by then was at the Western Reserve Medical School in Cleveland 30 miles away, to come and demonstrate his technique. Don arrived and connected his electrodes to Snodgrass amplifiers, while the lab group (Sperry, Joe Miller, H. D. Bouman, and I) watched. I can still hear those individual loud pops the loudspeaker emitted, which Don predictably adjusted down and up in rate by exerting less or more effort. In Stetson's opinon, "motor unit" meant one of the opposing muscle groups reciprocally activated around some joint to produce a ballistic movement, and Lindsley's different definition troubled him. But Sperry, whose master's thesis experiments mapped the sequence of the shoulder girdle muscle activations during such ballistic movements, welcomed the new techniques and ideas Lindsley brought.

After Lindsley's visit, Sperry and I fabricated concentric needle electrodes and invented new ones, the most successful of which was a strand of fine copper wire with a single line cut across its insulation with a scalpel blade. We threaded this wire into the eye of a surgical needle, passed the needle through our skin into a muscle and back out, and connected it to the Snodgrass amplifier and loudspeaker. When our muscle contractions caused the loudspeaker to emit loud pops, similar to Lindsley's, we knew the bared surface rested upon one or a few muscle fibers. I also found that an ordinary brainwave electrode placed on the skin over the first dorsal interosseous muscle—the one connecting thumb and forefinger—will readily pick up single units if one carefully adjusts the tension exerted.

My master's thesis proposal to the zoology department was the analysis of earthworm locomotion using muscle action currents recorded in Stetson's lab. Step one was to build a direct coupled amplifier; Snodgrass designed it, I built it, and it successfully amplified the potentials associated with earthworm movements, which we displayed with both a Westinghouse oscillograph and a smoked drum kymograph. My thesis was accepted in 1936, but it fell far short of what I had in mind. Stetson agreed to my remaining another year, at the end of which, still dissatisfied, I wrote my first paper, which was published in the Festschrift honoring him on his retirement (Galambos, 1939).

Throughout my six-year Oberlin stay I played saxophone in a dance band to help pay my bills, and when I left in the fall of 1937 for Harvard with the fellowship that made going there possible, I was a member of the musician's union abandoning a possible musical career for what I thought was going to be the life of a smooth-muscle physiologist.

Introduction to Neuroscience, Harvard I, 1938-42

At the Biological Laboratories I met my advisor, A. C. Redfield, a distinguished physiologist and oceanographer, and we worked out a course of study that included mycology and its delightful teacher, Cap Weston, and physiology, where George Wald made memorable comments such as "the Napoleon of smell has yet to be born," which I guess may still be true. Redfield gave me an office where I set up simple instruments for measuring the dynamic properties of invertebrate smooth muscles, and later arranged for me to spend the summer of 1939 at the Biological Station in Bermuda where my second, and last, contribution to smooth muscle physiology originated (Galambos, 1941a).

I told Redfield very early about my interest in electrophysiology, and with his blessing visited the Forbes-Davis Harvard Medical School laboratory for the first time during the 1937-38 winter. Alexander Forbes and Hallowell Davis welcomed me warmly, and before long I was making the trip from Cambridge to Boston at least once a week to serve as a subject in EEG experiments, or to watch other experiments underway, and even to lend a hand from time to time.

In the late 1930s the Harvard Medical School physiology department was one of a very small number of places in the world where students could learn electrophysiological techniques. For several years Forbes and Davis had aggressively supported development of the vacuum-tube amplifiers and stimulators that were propelling the department into the modern era of brain and peripheral nerve electrophysiology. Albert Grass, who designed and built all the physiological amplifiers and stimulators I used, succeeded E. Lovett Garceau, who had built the laboratory's first cathode ray oscillograph and EEG machine. Albert arrived a year or two before I did, and left in the early 1940s to found his famous Grass Instrument Company.

Several graduate students and postdoctoral fellows were measuring brain waves, evoked and cochlear potentials, and single cell responses (I recall A.J. Derbyshire, J.E. Hawkins, Jr., H.O. Parrack, B. Renshaw, and P.O. Therman). Birdsey Renshaw showed me my first fluid-filled glass pipette electrodes and explained how he had used them to record responses of single hippocampal brain cells *in situ* (Renshaw et al., 1940); he left, his thesis finished, shortly after I arrived. His equipment passed first to a postdoctoral fellow from Sweden, P.O. Therman, to whom Forbes apprenticed me in the 1938-39 winter. I inherited this set-up and used it with Hal Davis to produce data for the first two of our three papers on the cochlear nucleus—the ones erroneously called auditory nerve studies (Galambos and Davis, 1943; 1944). Our third paper is a disclaimer, four years later, that showed many of our electrodes must have been located in the cochlear nucleus (Galambos and Davis, 1948). To the detailed account of these experiments which appears elsewhere (Galambos, 1992a), I would add only the following advice to the eager graduate student or postdoc at an early stage of his or her career in neuroscience:

Do exactly what I did. Find yourself welcomed into a laboratory where, for the first time, one of the most important techniques of the century has just been shown to work. Learn to use the method from its pioneers. Then listen carefully as the laboratory director tells you the space and equipment will be exclusively yours into the indefinite future, and instructs you to make whatever measurements you wish. Your success is assured provided you remain, or become, diligent and attentive.

Micropipette Electrodes

I know of no scholarly history of the glass pipette microelectrode, but one or more may in fact exist (Stetson gauged the goodness of a paper by the quality of its literature review). Don Lindsley says the Forbes-Davis lab did not have them when he left the place in 1935, but two years later it certainly did, because Forbes, Renshaw, and Rempel described experiments using them at the 1938 meeting of the American Physiological Society (Renshaw et al., 1938).

Renshaw's pipettes were "pulled by hand or with a machine devised and kindly loaned by Dr. L. G. Livingston from thoroughly clean pyrex capillary tubing." After breaking the 3-5 micron tips to sizes "upward from 15μ," he filled them by suction with a warm agar-saline solution, inserted a chlorided silver wire into the cooled and hardened agar, and drove the electrode with a manipulator into the brain (cortex, hippocampus) of anesthetized or decorticated rabbits or cats, and chicken embryos (Renshaw et al., 1940). His microelectrode measurements may be the first ever made inside a living brain. In 1939, using Renshaw's technique, I prepared identical pipettes with 3-5 micron tips, filled them by sucking Ringer's solution up into them using a 20 cc syringe with its plunger coated with Vaseline, and inserted them into the cochlear nucleus area of anesthetized cats.

Ralph Gerard claims to have discovered, in 1936 with Judith Graham, the "true microelectrode" which he defines as "a salt-filled capillary with a tip small enough (up to five microns) that a muscle fiber could be impaled without excessive damage" (Gerard, 1975, p 468). The 1940 historical review in Renshaw et al. references the microelectrodes of Gelfan dated 1927, and of Ettick and Peterfi dated 1925, among others, but, curiously, not the Gerard and Graham version. A reprint Ted Melnechuk recently sent me describes a 3-micron saline-filled pipette used in 1918 by its author, I.H. Hyde; she calls hers a modification of one described in 1910 by Chambers, which in turn was based on the even earlier one of M.A. Barber (Hyde, 1921).

Gerard, in summarizing his career, says "I am probably best known for the microelectrode" (Gerard, 1975 p 474). Not by me. I remember him for the remarkable Gerard, Marshall, and Saul paper, the first comprehensive exploration of the cortical evoked potentials Richard Caton first described in 1875 (Gerard et al., 1936).

Bats

The collaboration with fellow graduate student Donald R. Griffin that pro-
duced my thesis experiments took place between May 1939 and November
1940, sandwiched in between a summer in Bermuda and the Davis audi-
tory microelectrode studies. It yielded six papers covered in my earlier
autobiography (Galambos, 1941b;1942;1943a,b; Galambos and Griffin,
1942; Griffin and Galambos, 1941). A paper just published adds details of
possible historical interest (Galambos, 1995a) and I am happy to say we
recently found the sound movies of flying bats taken in 1941, thought for
many years to be lost forever. Some advice: if your experiment is photo-
genic, take the pictures and remember where you stored them afterward.

By 1940, investigators had tried vainly for 150 years to discover the
mechanism by which blind bats avoid obstacles when flying. Today, in hind-
sight, it is easy to identify the two completely unrelated technical advances
that made the solution inevitable. One was the cochlear microphonic
method for testing animal hearing, which Hal Davis was teaching me; the
other was the development of the instruments that generate, detect, and
analyze high-frequency sounds inaudible to man. Don Griffin, a graduate
student already an authority on bats, had just published a paper reporting
they utter high-frequency cries inaudible to man; his co-author, G.W. Pierce,
a physics professor, had just invented the ultrasonic sound generating and
recording instruments essential for the demonstration. Don asked me to
test bat ears with the Davis method and within a month I had convinced
myself that the bat's upper hearing limit was an octave or more above that
of other animals. Don and I then designed and performed the behavioral
experiments that convinced us we had solved the problem. My recent his-
torical account of those experiments concludes as follows:

> Griffin and I were lucky, first of all, to have found each other,
> for it is not likely that either of us would or could have made
> the measurements alone. Then there are the facts that the lab-
> oratories of Professors Pierce and Davis were separated by a
> few miles, and that their doors opened wide to us the moment
> we knocked. And finally, every one of our experiments worked
> out exactly as planned, and they all pointed directly at the ear
> hypothesis Jurine, and then Spallanzani, knew to be correct
> (in 1795 they both agreed that bats with plugged ears collide
> with obstacles, but neither could say why this was so). At the
> moment we were united with our professors there was only
> one place in the world where two graduate students could
> demonstrate that flying bats emit sounds we cannot hear, and
> that the animals hear and act upon the echoes—and we hap-
> pened to be there (Galambos, 1996).

A graduate student once asked how I found the bat problem that became my Ph.D. thesis. Frankly, I cannot decide whether I found the problem or the problem found me. I favor the explanation that countless interrelated events, accumulated over 150 years, finally converged on the two of us, and that we, like bubbles in the vortex twisting around the drain of an emptying bathtub, swirled faster and faster along with Spallanzani, our two Harvard professors, and the many others who have left a mark in the literature. In this figure of speech, the problem disappears when the drain empties; however, 55 years later, according to my Medline search, about 25 bat hearing papers are being published every year.

Alexander Forbes

It is not easy to find words to describe the enormous changes in research methods my generation has seen. Let me try with the story of how one of my mentors, Alexander Forbes, came to work, and the equipment he used when he got there.

Alex was about to become emeritus professor of physiology at the Harvard Medical School when we met. He lived in the Blue Hills section of Milton, a Boston suburb. Around 1910, as a young faculty member, he rode to work on horseback, stabling his animal during working hours in a barn on Huntington Avenue near the medical school. During the wartime 1940s, as a member of a mapping expedition organized by the U.S. Geological Survey, he piloted his own plane while taking pictures over Nova Scotia.

He was middle-aged when someone discovered how to amplify small electrical signals using the vacuum tube, one of the most significant events in the history of technology, an advance ranked by some even higher than the microscope and telescope in its importance to science. Every discipline from astronomy through zoology entered its modern era as soon as its measuring instruments included electronic circuits that create large voltages out of small ones. Certainly neuroscience would not be what we know without the voltage amplifiers in electron microscopes, computers, physiological stimulators, and so on.

Hal Davis states that in 1923 Alex "had already developed a capacity-coupled vacuum tube amplifier to increase the sensitivity of his string galvanometer, and was the first to employ an amplifier in a physiological experiment" (Davis, 1991). Around 1930, when Alex decided to modernize his system, his options were another string galvanometer or the new vacuum tube amplifier-plus-cathode-ray-oscilloscope system being used by adventurous neurophysiologists like Gasser and Erlanger in St. Louis. According to Davis, the deficiencies of the then-available cathode ray tube, whose moving spot of light could be seen only by a partially dark-adapted eye, led Forbes to select the string galvanometer, but Don Lindsley has told me it had no amplifier when Forbes used it in 1933. When I arrived five years later, a string galvanometer was nowhere to be seen in the Harvard laboratory.

In 1939, when Alex added my name to the report that introduced me to glass microelectrodes, Albert Grass had only recently completed our stimulus and recording systems, a "thyratron set similar to the one used by Renshaw" and "a capacity-coupled push-pull amplifier connected with a cathode-ray oscillograph" (Therman et al., 1941). I measured the bat cochlear potentials with this amplifier, and within a week it was clear the bat ear generated frequencies well above the upper limit of Albert's amplifier response. A few days later, as I was moving the bat experiment to the Cruft Physics laboratory and G.W. Pierce's unique high-frequency system (Noyes and Pierce, 1938), Albert told me he felt betrayed. He had asked Davis and Forbes what the upper frequency limit of the new amplifier should be, and when they said 20,000 cycles per second he knew they would shortly want more, so he arbitrarily raised the upper limit to 40,000, which, as the bats revealed, was still not enough.

What about funding? Who paid for salaries, supplies, overhead? Alex bought his own equipment and supplies, and donated his $600 yearly salary along with even more princely sums to the department anonymously. The word overhead entered my vocabulary in the late 1940s, at which time universities considered one percent a welcome bonanza. In the mid-1950s, when I was doing my duty on study sections, I sometimes saw the same proposal twice, once at a meeting of the agency that paid overhead on salaries only, and again at the meeting of the agency calculating it on equipment and supplies only. Dishonest people turn up everywhere, but in a long career I have actually known only two crooks who invented their data.

Alex Forbes was a pioneer American electrophysiologist; like me, he loved the laboratory and continued working in one long after official retirement. Wallace Fenn's summary of this gentle man's many contributions is a beautiful tribute (see it in the *National Academy of Sciences Memoirs*, Vol. 40).

Hallowell Davis — Loud Sounds and Hearing Loss

In 1942, just after the Pearl Harbor attack, Hal Davis was offered the following assignment: find out how much and what kind of sound it takes to injure or incapacitate a man. A lifetime conscientious objector, he resigned his membership in the Society of Friends and accepted the assignment (Davis, 1991 p. 12). Hal collected the four of us listed as co-authors of his 1950 monograph "Temporary deafness following exposure to loud tones and noise" (Davis et al., 1950), and we proceeded to expose our ears to the sound waves emitted by a so-called bullhorn, the kind of loudspeaker the Navy used to deliver messages to personnel wearing earplugs on the busy flight deck of an aircraft carrier. We systematically varied the three sound variables—intensity, frequency, and duration—producing in ourselves increasingly larger temporary hearing losses, until we neared combina-

tions we thought might cause a permanent loss. At the end of the project, Hal decided to find out if our predictions were correct, and told us to expose his right ear—we always protected his left ear—to a wideband noise at 130 dB for 32 minutes. As predicted, this exposure permanently sliced a few hundred Hz off the high end of his existing congenital hearing loss in the 3500-3800 Hz region. The monograph that summarizes this work is still quoted in the literature.

Hal began wearing hearing aids in 1979, I in 1985. We agreed those wartime exposures had nothing to do with our presbycousis. My evidence seems particularly strong: we exposed only my left ear, but my measured losses have always been symmetrical, and I invariably put the telephone to my left ear, the one that took all the beating, because I "hear better" on that side.

Hal called his last research project "Old Time Ears." In 1990, he convinced 15 aging hearing specialists to join him in systematically documenting the progress of their hearing losses by all available tests, and recruited Charles I. Berlin and Linda Hood at the Kresge Hearing Research Institute of the South in New Orleans to administer them. In late 1995, all of us except Hal had our hearing tested once again in New Orleans. Hal discharged his final obligation to the project in 1992 when his temporal bones reached the Temporal Bone Bank in Boston for histological analysis.

The Origins of Neuroscience — Clifford T. Morgan and F. O. Schmitt

Morgan is one of the co-authors of the Davis temporary hearing loss monograph. In the summer of 1942, Hal sent the two of us to Woods Hole to find out whether underwater explosions are hazardous for the ears. Some physicists were exploding bombs in the harbor there, and we were supposed to jump in and have our heads submerged when this happened. We spent several beautiful summer days taking turns jumping off the pier at the Oceanographic Institute. The plan required comparing before and after audiograms, and we began with blasting caps detonated at 50 feet or so. When we detected no losses following detonations so close that we were afraid we might be wounded by shrapnel, we began jumping in when the blasters signalled a bomb of theirs was about to go off. They supplied us with pressure data from their sensors, and I recall really impressive shock waves compressing my body, but neither of us ever recorded a hearing loss.

Morgan came to Harvard with his new psychology Ph.D. from Rochester University to work with Karl Lashley, but before long he was traveling throughout the country for the National Defense Research Council helping coordinate the efforts of different laboratories working on the same or similar wartime problems. We were close personal friends and laboratory colleagues. Morgan's Ph.D. thesis had shown certain behavioral seizures in rats to be audiogenic, not the product of frustration or anxiety as N.R.F. Maier had claimed; two of our joint papers used the bull-

horn, outside of official hours, to confirm and expand this point (Morgan and Galambos, 1942, 1943). We also made pitch and loudness measurements in man (Morgan et al., 1951), and in 1957-58 worked out a long and difficult chapter on the neural basis of learning for the first *Handbook of Neurophysiology* (Galambos and Morgan, 1960).

Cliff went to Johns Hopkins to chair its Psychology department in 1947 and resigned in 1958 when he could no longer tolerate the tedium of administration. A few years later, royalties from his *Introduction to Psychology* (1961) made him rich. He became peripatetic, and served without pay on the psychology faculties at the University of Wisconsin and the University of California at Santa Barbara. In Austin, Texas he was loosely associated with the University of Texas, helped found the Psychonomic Society, named it, and established and edited its journal until his untimely death there in 1976.

His *Physiological Psychology*, written in spare time during his war work, was published in 1943. In it he says, "the primary goal of physiological psychology is to establish the physiological mechanisms of normal human and animal behavior" (Morgan 1943, p vii). Its 26 chapters cover, in some 600 pages, nothing but, and essentially everything known then about, what we call neuroscience today. The following paragraph comes from the introduction to his third, 1965, edition:

> Perhaps no subject draws upon so many different sciences and their methods as does physiological psychology. Every sort of pure and applied scientist—mathematician, physicist, chemist, physiologist, pharmacologist, anatomist, neurologist, psychiatrist, electrical engineer, as well as psychologist—has been taking part in our subject in one way or another (Morgan, 1965, p 9).

It can be argued, and I do, that when Frank Schmitt three years earlier coined the word "neuroscience," he merely renamed an existing discipline hard at work doing exactly what he had in mind (the first *Physiologische Psychologie* was published by Wilhelm Wundt in 1873). Schmitt's early Neuroscience Research Program Associates, of whom I was one, are all specific examples of the physicists, chemists, and biologists on Morgan's list (Schmitt, 1990, p. 218). Frank and Cliff looked at the same thing through different goggles. I can imagine Cliff congratulating Frank on having recruited all those Nobel Prize winners to join the ordinary biologists, chemists, and physicists already trying their best to describe the brain correlates of learning, memory, thinking, motivation, and so on. Of course, this takes away nothing from Frank Schmitt's contribution to the effort; this remarkable man organized, promoted, and catalyzed much of what subsequently transpired. But let history note he was not, as some claim, the first to discover the need for extensive interdisciplinary collaborations.

By 1962, when Frank Schmitt invited me to join his about-to-be-organized Neuroscience Research Program (NRP), I had spent 10 years as a member of Dave Rioch's Walter Reed group, a historically important prototype of the modern neuroscience laboratory where department lines were deliberately blurred, and cross-discipline thinking, the hallmark of physiological psychologist and neuroscientist alike, was the rule. Furthermore, I had found a similar spirit of interdisciplinary interaction to be the way of life in the Magoun group in Los Angeles where I spent the summer of 1955.

Neuroscience at the conceptual, textbook, and laboratory levels may not have been new in 1962, but Frank's NRP certainly was. Its faculty, the Associates, spoke often and eloquently from the platforms he created for them. The electron microscope had just come of age; the molecular biology revolution was barely underway; neurochemistry was at its threshold of unprecedented growth; and the first cognitive evoked potentials had just been averaged by computers. Nothing like this had ever happened before, and the Associates told each other at Work Sessions and Annual Meetings how the new methods and data were transforming old concepts and creating new ones. Each was a world-class expert in his field, and the authority and elegance of their presentations made for memorable learning experiences.

The origins and goals of Schmitt's NRP can be traced directly to his earlier response, in the mid-1950s, to the National Institutes of Health authorities who asked him "What is biophysics?" He answered, in 1958, by organizing a month-long "Intensive Study Program" (ISP) in Boulder, Colorado, at which 61 experts delivered lectures which were published in 1959 as the *Biophysical Sciences—A Study Program*. This book defined the field for the first time and was instrumental in the creation of the Biophysical Society.

A few years later, Schmitt found himself "interested in the possibility that information might be transferred in the brain and central nervous system not only by electrical action waves along neural nets, but also by fast transport, possibly through extracellular substances" (Schmitt, 1990, p. 201). In order to organize the effort to find out whether the brain actually does work this way, he simply elaborated and extended the procedures that had so successfully settled the question, "What is biophysics?" He conceived, organized, and funded what came to be called the Neuroscience Research Program. He selected experts, the Associates, to advise him on how to proceed, assembled a staff, and installed it in excellent quarters. Because "fast transport" was prominent in his hypothesis, his original 27 Associates included many with special knowledge of, or interest in, the fast transfer of elementary particles (electrons and protons) in solids and water solutions; five of them were pure physical chemists, and fully two-thirds were primarily physicists or chemists. He also began planning a month-long neuroscience ISP at Boulder and con-

vened it in 1966. This time he raised the number of experts delivering lectures to 65. Their contributions appeared a year later in what has been called the bible of Neuroscience, the first of the four volumes of *The Neurosciences: A Study Program*. Interestingly, only about a third of the book deals with the particular molecular biology questions that initially attracted Schmitt to the field.

The four *Study Program* volumes received world-wide acclaim as authoritative definitions and periodic updates of the field of neuroscience. Schmitt's NRP will also be remembered for its *NRP Bulletins*, which were conceived by Ted Melnechuk, an interdisciplinary writer who joined the staff in 1963 as director of publications to help plan the Boulder ISP. Ted immediately suggested that the Associates pinpoint the new findings and ideas that might become topics on the Boulder program; then invite a dozen world-class experts to a Work Session where one of the topics would be discussed; and then prepare and disseminate an edited version of their deliberations and conclusions. His ideas were accepted, and six such Work Sessions per year were promptly authorized; the first ones covered such neuroscientific vanguards as biomolecular information storage, the synapse, cell membranes, glial cells, brain correlates of memory, mathematical concepts of CNS function, and immunoneurology (a word, like "neuroscience" itself, first promulgated in the *NRP Bulletin*). Between 1963 and 1972 the *Bulletins* clarified the conceptual and empirical state of research in 75 such neuroscience subfields. The *Bulletins* became very popular, and reached thousands of practicing and potential neuroscientists and science libraries around the world (few know about the two-day Work Session on Extrasensory Perception I attended in the early days of the NRP; a *Bulletin* reporting it out was considered but rejected. Frank would try almost anything in his search for enlightenment).

During my 20-years as an NRP Associate I attended all four Boulder meetings and coauthored three of the *Bulletins*, all made possible by Frank's vision, hard work and extraordinary executive abilities.

Medical School and Military Service

My best friend, when I was 10 years old, was named Wilfred Earl Allyn, Jr. His father was a doctor, and we occasionally snuck into his home library to look at the pictures in his books. It was during this period of my life that I first wanted to be a doctor. Later, after reading Paul DeKruif's *Microbe Hunters*, I had to be.

At Oberlin I was a premed major, but on graduation, in 1935, in the middle of the depression, financing a medical school education was out of the question. But the yearning would not go away, and finally, in 1942, my wife Jeannette and I decided it was now or never. Obviously the dream could come true only if she went to work to support three of us, which she

did. I was accepted at the University of Rochester School of Medicine. World War II was on, and I enlisted as a First Lieutenant in the Army Medical Service Corps. The war and my medical school education ended at almost the same time without my ever serving a day in uniform.

But there is more to this military history. In 1952, during the Korean War, the draft board called my number. I reported for the physical examination, passed it, and prepared to receive marching orders. These never came, and I later found out why. The Army had neglected to discharge me from the Medical Service Corps, which meant I had technically been a soldier for more than 10 years. The automatic advances in rank along with other perks due me would mean inducting me as perhaps a Lt. Colonel entitled to a bundle of accumulated back pay, which made sense to no one.

At Rochester I was involved in several experiments, of which only one reached publication (Fenn et al., 1949). Other experiments included microelectrode penetrations of the cat optic nerve with Karl Lowy in the psychology department; rectal feeding of paralyzed poliomyelitis patients in the iron lung; and, with Jose Barchilon, the treatment of acute poisoning by the mushroom *Amanita phalloides*.

I interned in medicine at Emory University Hospital in Atlanta, and for another year debated, while teaching anatomy to medical students there with Harlow Ades, whether to practice medicine or return to the laboratory. The laboratory won out, and I had to choose between the Wilmer Institute in Baltimore and the Psychoacoustic Laboratory (PAL). The PAL was S.S. (Smitty) Stevens' wartime lab in the basement of Harvard's Memorial Hall, now newly civilianized but still funded by the Office of Naval Research. When I asked Smitty why he wanted me to come, he said that the war had consumed all our basic knowledge about hearing, and we needed pure research to generate more before the fighting began again.

Harvard II, 1947–51

My plan was simple. The cats and I would converse, with me asking the questions by delivering clicks and tones to their eardrums, and they replying, one brain cell at a time, through a microelectrode. No theory, no preconceptions; just simple experimental facts. I adopted this stern position because, as recounted elsewhere (Galambos, 1992a), Hal Davis and I had found inhibition in the auditory nerve, a totally unexpected event neither teachers nor textbooks had prepared me for. A pox on both their houses. Teachers and books peddle dogma, the enemy of discovery, and from now on I would believe only what I could coax the cats to tell me (actually, as will become clear shortly, most of our electrodes had certainly rested in the cochlear nucleus, not the nerve, and had I known this there would have been no reason for disillusion).

A dozen publications came out of my second Harvard period, one or more with collaborators Reg Bromiley, Ira Hirsh, John R. Hughes, Larry

Kahana, Cliff Morgan, Jerzy Rose, Walter Rosenblith, Mark Rosenzweig, and Carroll L. Williams. Of these, the three with Jerzy Rose on the medial geniculate consumed the most time and effort. We mapped the location of responding units in that nucleus, and whether they responded to clicks, noise, or tones delivered monaurally and binaurally. Jerzy liked my microelectrodes and carried samples back to Baltimore scotch-taped inside the rear window of his car. Vernon Mountcastle told me recently those highimpedance pipettes did not work with the Baltimore low input-impedance amplifiers, whereupon Jerzy devised the famous Dowben-Rose metal version and the Johns Hopkins laboratory entered the single unit business.

I did most of the writing on the medial geniculate papers, and when we sent them to the editor in 1951 I told Jerzy I was deeply disappointed at how little we had learned after so much effort. Jerzy, who had practiced psychiatry in the Pacific during World War II, sought to soothe me with this reply: "Maybe so, but these will soon be the best papers on the medial geniculate ever published." He knew they had to be, because for several years there were no others.

Cat experiments were a small fraction of what went on at PAL. E.G. Boring, the department chairman, invited us to bring our brown bags and join him at lunch every day around a huge oval table. George A. Miller, J.C.R. Licklider, and Ira Hirsh, among others, were beginning to become famous. My youngest daughter spent her first year in the Skinner crib George and I built, more or less overseen by B.F. Skinner himself, in the laboratory shop. Rufus Grason and Steve Stadler soon graduated from that shop to form their company that sold the amplifiers and audiometers they had learned to perfect, and along with another graduate, Ralph Gerbrands, the first generation of operant conditioning timing and recording equipment. Walter Rosenblith kept talking about the NIH-financed computer being built nearby, at MIT's Lincoln Laboratory, to process physiological data like what he, Mark Rosenzweig, and I were coaxing out of our cats, but to me the computer was an unnecessary distraction. I was still trying to find the data worth processing.

Bekesy

Georg von Bekesy was brought to PAL in 1947 by Smitty and E.B. Newman from Sweden, where he had gone after leaving Budapest at the end of World War II. When I arrived, he was setting up to continue the basilar membrane measurements for which he would receive the Nobel Prize. He was a quiet man, a bachelor, who rarely contributed to the wordy interplay at Boring's table. His 83-item bibliography cites only three co-authored papers. I remember him laughing only once. We were talking with a visiting scientist for whom I tried to explain something in

my high-school German. I noticed Bekesy laughing, with his hand held over his mouth, and when I asked him later what had been funny he said my German has a strong Hungarian accent (I learned my limited vocabulary of Hungarian words as a child overhearing conversations between my parents and others).

Don Griffin says the Yale bat man, Alvin Novick, visited Bekesy in 1953 or 1954 to seek advice on bat hearing matters but left without any. Bekesy was skeptical about the whole echolocation idea and said the emitted sounds were probably just noise bursts. A few years later after attending a seminar given by a visiting bat man from Brown University, Jim Simmons, Bekesy was heard to say maybe there was something to the idea after all. Bekesy and I saw each other almost daily for four years, but we never once talked about bats. Is it possible he had not read the bat papers published 10 years earlier?

Another strange thing. In 1947, I came upon a brief report (in a journal I have since been unable to find) of microelectrode experiments Bekesy and a person named Hamburger had done on the cat cochlear nucleus in Sweden. They confirmed our 1943 results and in addition demonstrated histologically that their electrodes had been in the cochlear nucleus, not the auditory nerve as Hal Davis and I had claimed. Our note in *Science* saying we had discovered this embarrassing fact ourselves had just appeared (Galambos and Davis, 1948). When I asked Bekesy why he had not told us he knew it all along, he said our experimental findings had been correctly reported, and he believed one should not emphasize the mistakes in a publication unless they alter the data.

We collaborated in only one measurement. His question was what an eardrum looks like as it ruptures. I exposed the eardrum of an anesthetized guinea pig from the inside by removing the wall of the bulla, and we adjusted the lens of a Fastax camera so that the eardrum filled a 35mm movie film frame. Fastax cameras can run thousands of frames past the lens every second. Bekesy fixed things so that the camera began rolling a moment before a starter's pistol fired a cartridge next to the pig's ear. Everything worked. The eardrum shatters into fragments that fly in all directions. The pictures were spectacular, but I don't remember why Bekesy wanted them or what has happened to them.

One Sunday afternoon I accompanied him to the Boston Fine Arts Museum. He had an appointment with the egyptologist, who took us to a basement storage area to see the items Bekesy had in mind. Bekesy collected such things and willed them all to the Nobel Foundation. He told me that when he received his Prize he visited the King of Sweden in his office, as was customary, and when he saw an Egyptian artifact on the shelf behind the King's head he commented on it, whereupon the two of them spent an hour talking about the hobby they shared.

Bekesy was also a historian-philosopher of science. For instance, he classified experimental problems in the following concise and amusing way:

> Problems arise in a variety of ways, and it is often worthwhile to list the forms that they may take. Thus we can distinguish the following:
> 1. The classical problem, which has had much effort expended upon it, but without any acceptable solution.
> 2. The premature problem, which often is poorly formulated, or is not susceptible to attack.
> 3. The strategic problem, which seeks data on which a choice may be made between two or more basic assumptions or principles.
> 4. The stimulating problem, which may lead to reexamination of accepted principles and may open up new areas for exploration.
> 5. The statistical question, which may be only a survey of possibilities.
> 6. The unimportant problem, which is easy to formulate and easy to solve.
> 7. The embarrassing question, commonly arising at meetings in discussion of a paper, and rarely serving any useful purpose.
> 8. The pseudo problem, usually the consequence of different definitions or methods of approach. Another form of pseudo problem is a statement made in the form of a question. It also is often the result of discussions in meetings (von Bekesy, 1960, p 5).

The most personally gratifying of my experiments fit into every one of Bekesy's first four groups. His 'classical' means to me that many people have already tried without success; his 'premature' means those unsuccessful predecessors had been denied an essential fact, concept, technique, or instrument without which the problem cannot be solved or even posed; his 'strategic' means you suddenly realize you can lay your hands at last on exactly what those predecessors needed and did not have; and his 'stimulating' means your contemporaries contemplate, replicate, and extend your findings. Here are two that fit this description.

> The bat hearing experiment with Griffin was premature for fully 150 years, but when instruments that generate and detect ultrasonic sounds finally joined hands with the cochlear microphonics method, the experiment became strategic. This is the scientific equivalent of saying you can't win a horse race if you don't have a horse, and then finding the horse.

The idea of studying single auditory neurons changed from premature to strategic as soon as someone could lock a newish tool, the microelectrode, into a micromanipulator, then connect it to another new tool, the right kind of amplifier, and then insert the electrode into the cochlear nucleus of an anesthetized animal. The first of those measurements converted some long-standing theoretical controversies into matters of historical interest.

Industry? Government? Academe?

The Harvard "up-or-out" edict hit PAL hard when the administration ruled that researchers not promoted "up" to permanent positions from temporary ones, like ours, would be "out" at age 35. We didn't want to go, but of course we did, seeding the entire U.S.A. with Smitty Stevens' ideas. We had no trouble finding jobs; very few with our training were available to fill the increasing number of post-war openings. My final choices narrowed down to either a government civil service job in Washington, D.C., or a position near the bottom of the academic ladder at either Iowa City or New York City.

Then, and now, most scientists blend various amounts of research, teaching, and administration within an industrial, governmental, or university setting. I chose the Walter Reed Army Institute of Research for three reasons: to gain experience in administration (ultimately for a staff of some 30 anatomists, physiologists, and technicians); to do research with abundant support in the company of productive colleagues; and to spend time, as a citizen, on my country's business. All these expectations were abundantly met during more than ten productive and exciting years.

David McK. Rioch and His Division of Neuropsychiatry—
An Early Multidiscipline Laboratory, 1950–61

The Rioch organization came into being because the Army wanted to solve a pressing practical problem. The Commandant of the Walter Reed Army Institute of Research, Col. William Stone, defined it when he interviewed me for the job. He said, in effect, psychiatric casualties had reached the top of the Army's list of medical problems, and Rioch's mission was to supervise the basic research effort that would drop it to the bottom (Col. Walter Reed had done exactly that for yellow fever 50 years earlier in Panama). Dave Rioch was a practicing psychiatrist highly respected in the Washington, D.C. area, a Johns Hopkins M.D. known for his anatomical studies of the cat thalamus, and a natural person for the army to select. Rioch, interpreting his mandate in the broadest biological terms, put on paper a Neuropsychiatry Division with, initially, departments of psychiatry; clinical psychology; experimental psychology; and neurophysiology, and began to

recruit the department heads. At our peak, we totaled well over 100 bodies, including technical help; we were an interdisciplinary group of practicing neuroscientists (not yet so-named), part civilian, part military, bent on making important contributions to knowledge about the brain.

I was one of Rioch's first appointments, in neurophysiology, followed within months by Capt. Joseph V. Brady (experimental psychology), and Capt. Harold L. Williams (clinical psychology). Rioch selected my first recruit, the young neuroanatomist Walle J.H. Nauta, imported from Switzerland. Rioch was a superb administrator, and therefore an expert at bending bureaucratic regulations; Civil Service had no classification called neuroanatomy, so he identified Walle as a "neurophysiologist (neuroanatomy)". Rioch filled many research positions by obtaining the names of M.D. and Ph.D. draftees from headquarters and telling his department heads to choose the ones they wanted. This meant many excellent young investigators spent their two-year duty-tours as Army officers assigned to do postdoctoral brain research.

Microelectrodes Again

Rioch hired me to do microelectrode experiments, but only about a third of the more than 180 papers and abstracts my group published fell into this category (the microelectrode group included Michelangelo G.F. Fuortes, Robert G. Grossman, David H. Hubel, George Moushegian, Allen Rupert, Johann Schwartzkopff, Guy Sheatz, Felix Strumwasser, and Vernon G. Vernier). I was particularly pleased with the superior olive study with Schwartzkopff and Rupert (Galambos et al., 1959), but surely the most notable of them all are the first six of David Hubel's visual cortex papers that later impressed the Nobel Prize committee. Hubel and I co-authored a different one: it describes auditory cortical cells that respond only to the sounds the cat is attending (Hubel et al., 1959).

Jerzy Rose and I returned to the cochlear nucleus study begun at PAL with John Hughes. During 1956-57 Jerzy would commute from Baltimore every week or so, often driving back after midnight; he insisted on perfusing the cat himself, to be sure the electrode tracks would show up well. The cochlear nucleus is a complicated structure divisible into three morphological regions in each of which the cochlea is unrolled systematically. Our report, which matches the nucleus itself in complexity, includes 29 figures, was published in a journal few libraries carry, and has been relatively infrequently referenced. Papers can be too difficult for readers to find, and, once found, too prolix and complex (Rose et al., 1959).

Implanted Animals — Labile Event Related Potentials (ERPs)

In 1953, when we learned of James Olds' self-stimulating rats, Brady and I went to Rioch with the suggestion that we take up that line of investigation.

His comment: "You two are running this show; if that's what you want to do, do it." We promptly invited Olds to come to Washington, and after he told us what he knew, Walle Nauta introduced him to the limbic system, the part of the brain into which he was placing his electrodes. The Olds visit was responsible for the dozens of studies on implanted rats, cats, and monkeys that became the trademark of Rioch's unit. As my fascination with the electrical responses delivered by these unanesthetized, intact brains grew, my interest in the microelectrode experiments on which I had spent 20 years declined. Rioch once pointedly told me he regretted this.

For some six years thereafter Guy Sheatz, Allen Rupert, and I implanted electrodes in monkey cortex and throughout the cat auditory system from the round window to the cortex, publishing more than 30 accounts of the various results. Toward the end I discovered computers at last, and with Sheatz, demonstrated a brain response I was sure deserved documenting—the transformations in amplitude and configuration of the cortical potentials evoked during behavioral conditioning in monkeys. As noted elsewhere, the Russians discovered the labile event-related brain potentials, but we were very close by when it happened (Galambos, 1995b).

Lesions

An early recruit to my unit was Capt. Leon Schreiner, a neurosurgeon plucked out of the Magoun group while it was still at Northwestern University in Chicago. Rioch soon had him removing the amygdalae of cats and monkeys to produce and study the Kluver-Bucy syndrome, a bizarre "psychiatric" disorder characterized by docility, hypersexuality, and odd, compulsive oral behaviors. The Johns Hopkins physiologists Philip Bard and Vernon Mountcastle had for some time been making such lesions and reporting their animals became more aggressive, not more docile. After a particularly vexing interchange with the Hopkins group, Schreiner queried some animal trainers who told him the only animal too aggressive to handle was the southern lynx, a cat about half the size of a lion. He ordered our Army veterinarians get him one, removed its amygdalae bilaterally and took moving pictures a few days later showing the animal wandering sedately and unrestrained through the hallway, rubbing against his leg in the typical feline manner, and eating chunks of raw hamburger out of his hand. The pictures settled the matter, as far as Schreiner was concerned, and he and Pvt. Arthur Kling, his draftee collaborator, published the experimental results (Schreiner and Kling, 1956).

Another drafted lesion maker was Capt. Ronald E. Myers, who arrived just after receiving his Ph.D. from Roger Sperry in Chicago. In his thesis he reported that cats with midline transections of both optic chiasm and corpus callosum could not perform a visual pattern discrimination learned through one eye when tested through the other eye; normal cats

do this with ease. At the Walter Reed, Myers extended this finding to the chimpanzee and to tactile learning. He taught them to use one hand to open the door of a small box containing a piece of banana; the task was difficult because hooks had to be unhooked, latches unlatched, knobs turned, and so on, and the animal was prevented from seeing what was going on. The normal animal could immediately open a mirror-image of the box with its untrained hand, but the chimpanzee with corpus callosum sectioned had to learn the task all over again.

Myers, Allen Rupert, and I collaborated on a different problem: what electrophysiological and behavioral changes follow cutting Cajal's classical auditory pathway at the point where it enters the thalamus? The remarkable answer is very few (Galambos et al., 1961; 1992a), a conclusion I still find difficult to believe. At Yale, as will be described shortly, we uncovered equally surprising facts following the comparable visual lesion.

Miscellaneous

The Olivocochlear Bundle (OCB). In 1949 I visited Grant Rasmussen in Buffalo to learn more about this collection nerve fibers he had discovered leaving the brain to innervate the cochlea. Anatomists generally ridiculed his claim, and he was always happy to talk to someone, even a physiologist, who did not. As already noted in detail (Galambos, 1992a), my Walter Reed research produced some physiological ammunition he could lob at the disbelievers (Galambos, 1956), but Moushegian, Rupert, and I failed, after several years of trying, to describe the role Rasmussen's feedback fibers play in converting basilar membrane mechanical movements into sensations of sound. Apparently their function is still poorly understood. My recent literature review reveals that the system is complex, not simple. Its feedback loops are now known to be multiple and to originate as high up as the cortical level; the efferent bundle delivered into a given cochlea contains fibers from at least four different places in the brain. It terminates differently around the inner and outer hair cells where it produces both slow and fast effects. Worst of all, a patient could hear equally well through each ear on a large and sophisticated battery of tests after the bundle entering one of the ears had been completely cut across. If ever a classical problem awaited the insights of the person who will make it strategic, this is it.

The Moscow Colloquium. October 6–11, 1958. The Academy of Sciences of the USSR organized and financed this meeting attended by 49 representatives from 17 countries to discuss "electroencephalography of the higher nervous system." A supplement to the *EEG Journal* published the 28 papers presented (Jasper and Smirnov, 1960). The official U.S. delegation consisted of M.A. Brazier, H.W. Magoun, Frank Morrell, and me; Herbert Jasper was Canada's representative. We participated in the first

face-to-face encounter between Soviet and Western physiologists in decades. The Soviet physiologists, despite years of government-dictated isolation, were familiar with our new ideas; it was instructive to hear them incorporate these into Pavlov's framework in public and to learn what they really thought in private conversations. Important as these interpersonal encounters were for the participants, perhaps the meeting will be remembered longest as the birthplace of the International Brain Research Organization, IBRO.

The Aplysia Parabolic Burster. The circadian rhythm in this single cell was discovered by Felix Strumwasser in 1961 at the Walter Reed Institute. It is, I believe, the first glia-neuronal system shown to continue its diurnal cycling when transferred into a petri dish (Strumwasser, 1963). In a modern version of his experiment the rat suprachiasmatic nucleus clock similarly survives *in vitro*, producing its 24-hour rhythm spontaneously for at least three cycles (Prosser et al., 1994). The possible glial contributions to this mammalian circadian clock is under active investigation (Prosser et al., 1993).

Sleep Deprivation. Rioch favored interdisciplinary research and his department chairmen delivered it enthusiastically. When someone suggested studying people deprived of sleep in the mid-1950s, his entire organization mobilized behind the proposal. Seymour Fisher and I were the guinea pigs who went through the entire procedure before formal testing began. We stayed awake 53 hours, enduring repeated psychiatric interviews, behavioral and EEG testing, and the frequent drawing of blood samples for endocrine level and other measurements. At about this time, a disc jockey in New York logged 200 sleepless hours in a booth in the middle of Times Square; our Capt. Williams interviewed him and followed his progress as part of the study. The reports that came from this effort, in which several small platoons of army privates typically stayed awake for 100 hours in the successive replications, are a classic in the literature of sleep research.

Anesthetics. S.N. Pradhan was a pharmacologist at Howard University College of Medicine, an institution a few miles away in downtown Washington, D.C. He asked to join our research enterprise, and we welcomed him, as we did many others. The resulting publication may record the first use of an averaging computer to study brain changes during anesthetic induction and the subsequent recovery. Our stable of implanted animals were ideal subjects, and his expertise and interest added the necessary motivation (Pradhan and Galambos, 1963).

Other Research. My neurophysiology department included Nauta's neuroanatomy unit and, for a time, John Mason's neuroendocrinology unit; both of which were outstandingly productive. Joe Brady and Hal Williams, my counterpart heads of experimental and of clinical psychology, were close companions and confidantes. We were young and enjoyed each others' company; we almost never disagreed on administrative deci-

sions important to us all, and co-authored several papers combining behavioral, anatomical, and physiological measurements.

Glia I

I left the Walter Reed Institute after a falling-out with Dave Rioch over my sudden interest in glial cells. This is what happened.

During the afternoon of Friday, October 28, 1960, on an airplane somewhere between Chicago and the Grand Canyon, I turned to my companion, Harvey Savely, and announced, "I know how the brain works," and for the next hour or so bent his ear with the ideas published two months later in the paper, "A Glia-Neural Theory of Brain Function" (Galambos, 1961).

I share with everyone else the occasional experience of having the solution to a problem suddenly arrive unasked. This particular vision appeared at the end of some 15 Harvard and Walter Reed years occupied by work along four different lines—microelectrode recordings; brain changes during learning by implanted animals; auditory pathway lesions; and the efferent olivocochlear bundle. We had discovered many interesting things, but none of them seemed to bring me at all close to what I really wanted to know, which is the way animal brains store and retrieve phylogenetic and ontogenetic memories (Galambos and Morgan, 1960). My revelation both ended the frustration and pointed a way to the fresh ideas and experiments that might give answers at last.

What followed had for me profound personal and scientific consequences. Six months later I had found another job because my boss became so angry we could no longer work together. A week after the insight flashed into my head, I laid a draft of the paper I proposed to publish on Rioch's desk. He returned it promptly with a six-paragraph note suggesting I first do this with the paper, then that, and still something else. A few days later he had a copy of the final draft, which I saw sitting in the in-box on his desk, untouched, for over a week. We had several warm discussions during this period marked, among other things, by an order that I not discuss my idea at an upcoming seminar, as well as a prediction that my scientific career was over because I now had a theory and would spend the rest of my life proving it. After two months of this kind of thing, I was actively looking for another job.

Autobiographies sometimes tell of confrontations over teaching load, politics, bad habits, or personality differences. My confrontation with Rioch was over an idea. We had worked together harmoniously for a decade. His vision and administrative skill had conceived, created, and sustained the archetypical neuroscience laboratory; his department chiefs had put together a factory which, in less than a decade, had churned out dozens of first-class papers on topics ranging from microscopic anatomy to clinical psychiatry. Like everyone else at the time, and many still, we had

extrapolated Cajal's neuron doctrine to mean that neurons were the only cells in the brain worthy of study. I could at that time understand, and still do, how difficult it is to entertain a major challenge to one's dogma, but when Rioch ordered me not to talk in public about my new idea, I knew it was time for me to leave. I once told a student not to do a particular experiment, but he knew me well enough to go ahead anyway, and we were both pleased when it worked. But I didn't demand that he hide the idea, nor will I ever think highly of someone who would.

An attempt to transfer from the Walter Reed to another government job at the NIH failed when an unrelated (I think it was unrelated) confrontation not worth recounting here intervened. What remained were academic and industrial jobs. During the previous 15 years, I had turned down several university offers using the following reasoning: students come first in the university job, research comes first in the research institute job, so if you put research first you turn down the academic job. I went, finally, to Yale as the Eugene Higgins Professor of Psychology and Physiology, content to give second priority to what pleased me most. It consoled me to remember those bright and capable Ph.D. and M.D. draftees assigned to us at the Walter Reed—those people were once the golden eggs universities hatch, and this was my opportunity to incubate a few of my own.

Yale, 1962–68

Physiological Psychology (aka Neuroscience)

In 1962, the stimulus-locked electrical events recorded from the brain, ERPs, were called evoked potentials (EPs), and the manufacturer of the first commercial hard-wired computer designed to average them, the Mnemetron CAT (Computer of Average Transients), quickly became very busy indeed. My first act at Yale was to buy one—a wonderful, dependable device with several annoying features—and very soon after that I bought a second one. A year of so later, I bought a FabriTek Model 1052 (serial #2, and as of 1995 it still worked). These three computers were so popular you had to sign up to use one days in advance.

I favored hard-wired computers over general-purpose computers because they were easy to learn to use. I had noted that whenever a lab hired a programmer, he instantly became a kind of king who dispensed favors, whereas when my students and I obtained evoked-response averages by pushing buttons, we were the kings. Tools should work for you, not the other way around. I did encourage students to build at least one amplifier just to get a feel for instrumental complexities, but the amplifier they used in their thesis research was the finest commercial instrument I could buy.

The following is a list of the Yale research projects that used Grass amplifiers, both the free-standing and the EEG machine varieties, connected to these hard-wired computers:

ERP Lability. Warren O. Wickelgren's thesis became three papers demonstrating that ERP lability is confined to thalamus, cortex, and cerebellum. His cats were implanted from cochlear nucleus through auditory and visual cortex; they wore earphones and learned to walk on a treadmill in one of the most carefully controlled animal experiments I have known (Wickelgren, 1968).

Brain Refractory Periods. Luke M. Kitahata and Yoshikuri Amakata were postdoctoral fellows in Yale's department of medicine. They produced a successor to Pradahn's Walter Reed pharmacological study; they anesthetized implanted cats with halothane and measured the ensuing prolongations of refractory periods at brainstem, thalamic, and cortical levels (Kitahata et al., 1969). Recovery is prompt at the brainstem level and progressively slower at higher levels.

The Contingent Negative Variation (CNV). Steven A. Hillyard's CNV thesis yielded the publications that launched a distinguished career (for example, Hillyard and Galambos, 1967). He is one of those golden eggs I had expected to encounter as a professor.

The following entries identify the Yale experiments that turned out beautifully but left behind the conviction that brains still hide their best secrets. Two of these studies are typical classical problems awaiting the explorer unafraid to take big chances in hopes of big rewards.

The Evoked Resistance Shift (ERS). Kenneth A. Klivington's Ph.D. thesis satisfied both the engineering and the psychology department requirements. He delivered clicks to cats and measured differences in resistance between the two cortical recording electrodes in addition to the conventional ERP. A small resistance shift, with a slightly different time course, approximates the shape and duration of the ERP. Ricardo Velluti obtained similar results in subcortical nuclei of both the auditory and visual systems. We could not explain the ERS mechanism then, but today the flux of potassium ions through astrocyte membranes during synaptic activity seems likely. However, the problem still sits untouched a quarter century after it was defined (Klivington and Galambos, 1967; Galambos and Velluti, 1968).

Optic Tract Lesions. Thomas T. Norton and Gabriel P. Frommer, undergraduate and postdoctoral fellow, respectively, cut cat optic tracts in experiments aimed to discover the largest lesion that fails to impair performance on pattern discrimination tasks. To everyone's surprise, cats with less than two percent of the normal input to the lateral geniculate performed perfectly, a startling contradiction of the conventional expectations that remains unexplained. Completely severing both optic tracts produced total blindness, of course (Galambos et al., 1967; Norton et al., 1967). In a related study, Eli Osman used computer-averaged data to redo and confirm the Walter Reed

finding that unanesthetized cats with and without input to the medial genic-
ulates produce the same cortical click responses. I discuss these visual and
auditory findings elsewhere in detail (Galambos, 1992a). These results sug-
gest to me is that functional visual and auditory wiring diagrams differ great-
ly from the anatomical wiring diagrams our students learn.

An Implantable High Power Microscope. In 1964 the triumvirate,
Mojmir Petran, Milan Hadravsky, and David Egger joined me, supported
by my National Aeronautics and Space Administration (NASA) grant, in
attempting to devise a microscope through which we would view the move-
ments of normal cat brain cells *in situ*. I was powerfully motivated to
accept this challenge after viewing the remarkable time-lapse moving pic-
tures of cultured glial cells Gerald Pomerat had produced and was widely
displaying. Needless to say, we did not reach our goal, but we approached
it (Petran et al., 1968). In today's world the confocal microscope with its
laser illumination (we used sunlight admitted through a hole in the labo-
ratory ceiling) approaches what we had in mind,

Glia II

Before leaving the Walter Reed, I had considered several possible glial
research projects and settled on producing anti-glial antibodies which,
when introduced into the cerebrospinal fluid of cats with indwelling elec-
trodes, had been reported to produce morphological and EEG changes in
the recipient (Mihailovic and Jankovic, 1961). I initiated these antibody
experiments in 1963 at Yale, and invested close to half of my time, effort,
and NASA grant funds on them for almost six years. Exactly one abstract
(Galambos et al., 1966), one Ph.D. thesis (John Chimienti), and two stu-
dent term papers (Martin Stein, Robert Humphries) represent the tangi-
ble results. To the graduate student who asked how many mistakes one is
allowed to make during his career, I answer none at all, and then add that
if you must make one have it be really big, and save it until you hold a
tenured faculty position.

Goodbye Yale, Hello La Jolla

In all, my laboratory group published 41 papers during my seven-year
tenure as a Yale psychologist and physiologist. I also conducted the five
summer-long teaching sessions previously mentioned during which at
least 50 students ranging from undergraduate to associate professor in
rank learned some rudiments of electrophysiological techniques. Denis
Baylor was one of several golden eggs in this group.

I also joined with Jerome Sutin and a few younger members of the Yale
anatomy, pharmacology, and physiology departments in an attempt to create
a university-wide coalition of neuro-anatomists, neuro-pharmacologists, and

neuro-physiologists along the Walter Reed model. We failed; every depart-
ment head refused to relinquish the neuro- portion of his turf. Meanwhile,
in 1967 Robert B. Livingston began telling me about the department of neu-
roscience he was creating at the new University of California campus in La
Jolla. He and Theodore H. Bullock described just the kind of cross-discipline
organization I had in mind, and at their new Medical School there were no
entrenched department chairmen with turf to protect. They urged me to join
them; I was reluctant to leave my Yale responsibilities so soon after taking
them on, but I did.

The University of California, San Diego, 1968–82

The Department of Neuroscience

The first neuroscience department in the world was conceived by its first
Chairman, Robert B. Livingston, in 1964-65. Its responsibilities include
medical and graduate student instruction, the neurology resident program,
and the clinical neurology services in the hospitals operated by the univer-
sity. Its organizational details were worked out during 1967-69 by the chair
along with Theodore H. Bullock, A. Baird Hastings, Charles E. Spooner,
Charles Bridgeman, Theodore Melnechuk, and me. In due course, the
department also became the administrative unit of the Neurosciences
Group, which is now a university-wide voluntary consortium made up of
more than 80 professors from 14 university departments who will accept
graduate students seeking degrees in some aspect of brain science. For its
first dozen years, I was the group's director of graduate studies.

From the beginning, the department was planned to have equal and
interacting clinical and basic science arms, a controversial organization
scheme many predicted could not survive; a quarter century later it remains
in place, largely unchanged. In 1995, the National Research Council rated
our neuroscience graduate program number one in the United States.

Auditory Event Related Potentials (ERPs), Again

I moved all my research grants and paraphernalia from Yale to San Diego
and promptly put together a new animal laboratory. However, within a few
years I had abandoned animals, left microelectrodes, and embraced human
ERPs. There were three reasons for this move. First, the local antivivisection
opposition became increasingly strident, aggressive, and annoying. Second,
at a time grant money was becoming more difficult to get, I added together
the cost of maintaining an animal house, buying cats, caging and feeding
them for months, and paying the fees for mandated university veterinarian
services, and compared this sum with the $5 per hour pocketed happily by the

already-trained college sophomore who houses, feeds, beds, and doctors himself. Third, Terry Picton delivered a seminar presentation in which he plotted, for the first time on the same time base, the auditory brainstem, middle latency, and late slow waves, whereupon we all realized what we had thought of as three separate events was actually a kind of single unit consisting of some 15 distinct waveshapes awaiting dissection and analysis. For this kind of enterprise college sophomores would make ideal subjects.

In 1972 we decided to divide the auditory ERP into two parts, one including the newly-discovered auditory brainstem response (ABR), the other containing the waves beyond about 50 msec. The boundary was flexible. I fell heir to the ABR while Terrance Picton and Steve Hillyard took charge of the late waves (along with, as time passed, Eric Courchesne, Robert Hink, Howard Krausz, Robert Knight, Marta Kutas, Helen Neville, Vince Schwent, Kenneth and Nancy Squires, Elaine Snyder, and David Woods). When I retired in 1981, this late-wave group, which initially focused on the CNV and selective attention, had published cognitive ERP papers at a rate of six to eight per year and ranked with the best in the field anywhere. The ABR work at the Children's Hospital is described below.

Loudness Enhancement

Teaching a seminar on the auditory system was one of my responsibilities. Following our discussion of the mysterious olivocochlear bundle, my 1971 seminar group designed, performed, and published the following experiment. A listener receives, monaurally, two tones separated by an interval of a second or two, and learns to adjust the loudness of the second one to equal that of the first. This task is then repeated immediately after a short noise burst stimulates the opposite ear. Our idea was that the noise burst will deliver a transient olivocochlear pulse into the test ear, and this will change the apparent loudness of the first of the two tones. The result: subjects report the first tone sounds much louder (up to 35 dB) or much fainter, depending on the strength and timing of the contralateral noise burst (Galambos et al., 1972). Unfortunately, we failed in several subsequent studies to show the olivocochlear bundle is responsible for the phenomenon, and at the present time loudness enhancement and diminution remain unexplained in neuronal terms, another of Bekesy's classical premature problems. Robert Elmasian's thesis contains the relevant experiments, most of which have been published (Elmasian et al., 1980).

Microwave Hearing

I worked for several months during a 1975 sabbatical year at the University of Washington with C.-K. Chou and A. W. Guy on a number of the experiments Chou included in his thesis (Chou et al., 1982). Thirty years earlier,

during the war, it had became known that the pulsed microwaves emitted by a radar antenna are heard as a series of clicks by a person who puts his head in their path. The phenomenon was explained by some to be a result of direct stimulation of nerve cells, and by others as the perception of a miniscule pressure wave set up in the head as the absorbed microwave pulses are converted to thermal energy. My hosts, who were physicists, favored the thermoelastic expansion hypothesis, but they sought my counsel to discover whether they might be making a mistake. There was no mistake, as we established by cochlear microphonic and ABR experiments on cats and guinea pigs, and by demonstrating that the rat trained to press a lever for a reward when it hears clicks will press equally enthusiastically when its head is in the path of pulsed microwaves. The matter was finally settled when I realized I did not myself hear the microwave pulses the rats detected and visited the university audiology department, where an audiogram revealed my high frequency hearing loss.

My wife Carol Schulman and I spent five weeks of this sabbatical year in Japan as guests of several Japanese scientific organizations, introducing the ABR, which was so new no one there was using it yet. Jun-Ichi Suzuki, our host at the Teikyo University in Tokyo, provided us with an office in which we wrote the first manual to describe the ABR methods and illustrate its typical results. We distributed copies of the manual there and back in the United States on our return. At more than a dozen universities between Tokyo in the north and Fukuoka in the south, I wired together whatever local apparatus was available and successfully demonstrated the ABR, always using a young woman subject because we had already discovered that women's ABRs are almost always large and easy to obtain.

The Speech and Hearing Center at San Diego's Children's Hospital, 1972–92

Not long after arriving in San Diego in 1969, I paid a get-acquainted visit to the Speech and Hearing Center (which is not connected in any way to the university) and was warmly greeted by its director, Donald Krebs, and his assistant, Bob Sandlin. Both were interested in research and showed me their Princeton Applied Research Waveform Eductor, the first commercial computer designed to estimate auditory thresholds by averaging cortical late waves. A year or so later, they supplied the space in which Carol Schulman estimated the hearing thresholds of hard-of-hearing and diffi-cult-to-test children using her experimental heart-rate audiometer. When in 1972 I could find no clinical research space anywhere in the university for my graduate student Kurt Hecox, Carol suggested I take my problem to Krebs and Sandlin; within days, Kurt was setting up equipment in one of their soundproof rooms, and the extraordinarily happy arrangement that supported and nourished my laboratory for the next 20 years had begun.

The Auditory Brainstem Response (ABR)

As described elsewhere (Galambos, 1992a), my interest in objective tests of hearing dates from my Walter Reed days. While there, I helped develop two procedures aimed at identifying the malingerer who feigns hearing loss at the time of discharge in hopes of drawing an undeserved Army pension for life. Both of these tests reached the goal, but they were too complex to administer in busy clinical settings. A few years later, in 1963, Don Jewett, while my postdoc at Yale, discovered the cat ABR, and in 1971 published his classical paper with Williston on the human ABR in the journal *Brain*. When a preprint of this *Brain* paper circulated through our laboratory in 1970, my reaction was immediate. Was this ABR the objective hearing test I had been looking for—the way to resolve another one of those classical, premature problems?

The Children's Hospital wards and the Speech and Hearing Center, which are connected physically and administratively, are about 10 miles away from the La Jolla campus, but Kurt and Carol moved easily between them. They began ABR-testing babies in their Speech and Hearing Center sound booth, but before long Carol was also using a small room adjacent to the normal newborn nursery at Sharp Memorial Hospital, which is connected to Children's by a tunnel, and where some 6000 babies were being born every year. In 1973, Paul Despland joined the group from Lausanne, Switzerland, where he was the neurologist in charge of the EEG department. For a year he almost literally worked day and night in the Intensive Care Nursery (ICN) at Children's Hospital, which is a regional third-level intensive care center, a place to which the sickest babies born in the county are transported. It took the four of us several years to collect the basic science information needed to design and validate the clinical hearing tests we finally installed. We eventually published 19 papers that, among other things, established the age-dependent ABR norms for babies as young as 12 weeks premature, differentiated conductive from sensorineural hearing loss using the ABR, estimated the prevalence of hearing loss in the normal and intensive care populations, and convinced the audiologists that the ABR is a trustworthy way to approximate thresholds in difficult-to-test children.

By 1976, our pilot studies had repeatedly demonstrated that hearing loss is common in the ICN and exceedingly rare in the normal newborn nursery. Armed with these facts, we proposed to deliver the ABR test to all ICN graduates and to follow-up those found to have hearing loss at the Speech and Hearing Center. The hospital administration agreed, and in 1977 we installed the clinical program that has continued without interuption to the present day (Galambos et al., 1994). In 1996, our ABR program celebrates its 25th birthday, its original data acquisition methods unchanged, and the clinical program still under the supervision of Mary Jo Wilson, who has run it since 1979.

40 Hz

In 1978, when no commercial ABR machine was as yet for sale, an MD-Ph.D. candidate, Peter Talmachoff, designed and built one as his thesis project. When he first tested it on human volunteers, in 1980, he delivered clicks at a rate of 40 Hz and recorded the physiological responses through an amplifier with a bandpass wider than was customary; the recordings contained what we thought at first must be an artifact at the stimulus rate but turned out to be the 40 Hz physiological phenomenon we described in 1981 (Galambos et al., 1981). Scott Makeig, the last of my Ph.D. students, picked up where Talmachoff left off, produced his Steady-State Response (SSR) thesis in 1985, and in the process introduced me to the power of frequency analysis methods. We abandoned an attempt to develop an infant audiometer using 40-Hz tone bursts at the audiometric frequencies in 1988 when we discovered newborns do not reliably produce 40 Hz responses. Recently, the use of more sophisticated stimulus delivery and response analysis procedures by others has revived hopes that 40 Hz audiograms may soon be obtained from small babies after all.

What do these 40 Hz frequencies tell us about the brain's operations? I have written what I know, and it is not much (Galambos, 1992b). The 40 Hz contribution to that mysterious band of spontaneous and driven brain wave frequencies is small compared to the alpha-wave contribution, and my inability to answer the most basic questions about what generates either of them is a major embarrassment. I think it disgraceful that we all remain only a bit less ignorant of the mechanisms that create and modulate brain waves than was Berger, their discoverer, 65 years ago. Do they convey something interesting about brain functions or, as someone has suggested, is their message irrelevant, like the noise of the toilet as it flushes? Perhaps some useful answers will be forthcoming from the current research attention Makeig and others like Ted Bullock and Erol Basar are giving the problem.

Tending to Unfinished Business, 1992–Present

In 1992 I closed the door of my own laboratory for the last time, and no longer had a place to go after having worked in one almost daily for over 50 years. My domain is now a small room at home. Most of my books and journals have been donated to others, and the bulk of my papers are locked up in rented storage space several miles away. Since I have no secretary, I finally learned to type, and with my word processor have managed to get nine papers (five of them refereed) published from this place. Thanks to e-mail, I communicate almost daily with Gabor Juhasz in his Budapest laboratory to which I commuted three times in a recent year. His group and I are doing experiments on glial cells, and we are getting interesting results at last.

Glia III

Shortly after arriving in San Diego in 1968, I abandoned the Yale antibrain antibody project after failing to ignite any interest in the several Salk Institute immunologists who listened politely to my presentation. In retrospect, there were two strikes against the idea from the start—I did not know enough about immunology, and the purified astrocyte antigens essential for quantitative results did not exist. Today, specific anti-astrocyte antibodies could conceivably be prepared which, after injection into the cerebrospinal fluid of experimental animals, might produce the behavioral deficits and astrocyte lesions we were hoping to see 35 years ago, but more precise and elegant genetic methods would probably be used instead.

For almost 20 years I laid low, followed the glia literature, wrote two glia papers, one of them for a Rioch festschrift (Galambos, 1971), and waited for something to happen. It did, in 1986, when Juhasz approached me during the IBRO meeting in Budapest and suggested we work together on a glia problem. As already reported at length (Galambos, 1992a), our first experiments were inconclusive, but perseverance paid off in late 1993, when we prepared rats with electrodes implanted around the eyeball for recording the electroretinogram (ERG) and in the cortex for recording visual cortical ERPs. We also implanted a light-emitting diode under the skin over one eye for producing flash stimuli. The result is a normal, freely moving animal restrained only by the bundle of wires connecting a plug on its head to the distant stimulating and recording devices. Whenever we push the button that activates the rat's built-in stimulator, a flash of light evokes two potentials, one generated where the animal's visual system begins, the other where it ends.

The preparation is interesting because the first potential, the ERG, is widely conceded to index the intracellular transport of potassium ions in the Müller (glial) cells. The evidence supporting this conclusion, which others began accumulating some 30 years ago, can be very briefly summarized as follows: synaptic activity in retinal neurons raises extracellular potassium ion concentration; Müller cells uptake this excess and transport it away; the resulting intracellular-extracellular ion current loop appears outside the eyeball as the ERG. Does the rat's second potential, the cortical ERP, index a similar potassium ion flux through cortical astrocytes? We are attempting to answer this question by comparing the way the two responses change as we vary stimulus parameters and/or the state of the animal. Our first publication concluded that one cannot exclude the possibility that cortical astrocytes contribute to ERPs what Müller cells contribute to ERGs (Galambos et al., 1994). In reports now being prepared, we make additional comparisons that continue to support this conclusion. It actually seems possible that evoked potentials generated in synaptic regions throughout the brain will all turn out to be the joint product of the neurons and the glial cells that are invariably located nearby.

These results take me back to my 1961 glia paper which, in essence, is a suggestion that brain scientists should include the glia in the models they take into the laboratory. Increasing numbers of them appear to be doing this, to judge from the recent proliferation of glia papers. It may soon be neither wise nor tenable to think of the brain as an interacting collection of neurons. Electron microscope images show every brain to be a single system consisting of three interlinked compartments—neurons, glia, and extracellular space. The system does not function the way its genes intend unless all three parts are in place, at work, and in an unanesthetized animal. Much can be learned from drugged or dead brains, and from parts of it living in test tubes, but the most obvious message is that the operations responsible for integrated behavioral responses do not exist under such conditions. One sees behavior only when the real thing, its three compartments interacting harmoniously, works inside the container the genes have prepared for it. If behavior is what interests you, study the system out of which it comes.

Having delivered myself of this somewhat controversial theoretical position, let me continue with two more points of view some find even more distasteful. Let me identify, first, the preparations I think are most likely to yield answers to that lofty goal encapsulated in that hackneyed phrase "how the brain works," and then, second, say what I think we need to know about those behaving systems if we are to reach the answers we seek. It is customary today to single out the human cortex as the place to study how the brain works, but I do not share that view. I would work with the phylogenetic memories if my research career stretched out in front of me instead of behind me. Phylogenetic memories, like all memories, are products of the neuropil, where all behavior originates out of the interactions between its three compartments.

The Phylogenetic Memory

If I were to ask you to give me your mother's maiden name, you could do it, and then I could recite it back to you. Such commonplace exchanges show our cerebral cortexes are normal, and that we share the mechanisms that retrieve learned facts and deposit them into our unique memory stores. We also share what have been called phylogenetic memories, the species-specific behavioral repertoire created, like the shape of a finger, by our genes (Galambos and Morgan, 1960). Human newborns display dozens of these phylogenetic memories: babies start breathing at once, and know how to cry out when cold or hungry; they can suckle, swallow, digest food, circulate blood, empty the bladder, and do still other things. Later on, with little or no special training, they display the behaviors on which species survival depends—courtship, mating, and the care of the young.

For some animals the behavioral repertoire is almost entirely the product of these phylogenetic memories. Cockroach genes put together a nervous system that requires them all to scurry away when the kitchen light comes on in the middle of the night. Spider genes build a brain that creates what we call hunger, and makes possible the web-spinning that entangles the dinner, and the eating, digesting, and excreting behaviors that follow. Genes securely build good habits like these into the nervous system of every animal that takes in air and delivers it throughout the body; and for every ability to become thirsty, find water, and drink. The list of things animals do without instruction is very long, and it includes the ability to learn from experience, a habit so well developed in ourselves.

Most of us now writing autobiographies first grasped the connection between genes and all this biological behavioral machinery as adults, thanks largely to the gene technology elaborated after Watson and Crick's great discovery in 1953. Today the evidence for the primacy of the genes in determining form and function is overwhelming; it seems highly unlikely that any future disclosure will seriously challenge the proposition that genes create a brain for each animal that produces exactly the behavior patterns needed for survival in its ecological niche.

The Dedicated Neuropil

Neuropil is the term C. Judson Herrick used in the early years of this century for "the intricate tangle of thin unmyelinated fibers" his light microscope revealed in every synaptic region. Today he might agree to define neuropil as an organized system in which the three brain compartments interact harmoniously. Herrick considered neuropil to be the brain's "primary apparatus of integration" and its product to be "a total pattern of behavior." Today he might agree that samples of behavior such as drinking, digesting, defecation, and so on, are products of specialized regions of this neuropil—call them centers—within which unique interactions take place between inputs and outputs. The most obvious such center I can name is the retina, a typical neuropil made up of neuron and glial terminals separated by extracellular space, the whole of it dedicated to meet a specific biological need. Eyeballs containing a lens and retina similar to ours are found throughout the vertebrate phylum, which suggests that once genes devise a superb solution to a given problem they simply duplicate it, with small changes introduced here and there. My recent study of the rat retina has given me considerable respect for the contributions glial cells can make to such a functioning unit; the well-known neuron-neuron interactions in retinal neuropil play a key role in converting light waves into optic-nerve discharges, as do the Müller cell-neuron interactions going on at the same time.

A second example of the dedicated neuropil is the suprachiasmatic nucleus clock, which, as noted above, continues its 24-hour cycling in a

test tube when dissected out of the rat brain. I anticipate that, as in the retina, future measurements will uncover essential contributions from the glial compartment in this neuropil also, and further, that the glial cells around Strumwasser's parabolic burster *Aplysia* neuron will be found to make a similar contribution to the diurnal cycling found there.

Other dedicated neuropils include temperature center, respiratory center, hunger center, drinking center, sleep center—in fact, every neuropil region created by the genes to do a particular job well, such as the spinal cord territories where reflexes organize, and even the cortical columns, the neuropils of which have been prepared by the genes to store and release our "real" ontogenetic memories. In short, the typical species-specific behavioral response is a phylogenetic habit laid down by the genes in the form of organized neuropil. This thought can be extrapolated to its ultimate—the neuropil organization responsible for my sensations of hunger may well resemble the one in the spider that prompts the web-spinning that entangles its dinner, and the brain mechanism that causes air to leave and enter my body may have a recognizable counterpart in the insect neuropil that controls the same process.

In Herrick's time, there was no way to test ideas like these experimentally. He did not have the tool, the concept, that would make empirical testing reasonable; this was provided only a decade or so ago by the discovery of the homeotic and segmentation genes. That the same homeobox gene family determines the segmental organization of species as distant as *Drosophila* and mouse makes it reasonable to ask whether the two species similarly share one gene family that creates their ability to breathe in and out, and another that makes it possible for them to find food and eat. Can it be that the mechanism responsible for morphological universals has much in common with the mechanism responsible for behavioral universals? We will know the answer one day.

Coda

I greatly admire Ted Bullock, a close colleague for almost 30 years, in my opinion the wisest and most erudite of living neuroscientists. Both of us are what I call systems people, willing to take brains apart and even examine them cell by cell with microelectrodes, but the question of how the parts fit together in the behaving organism is never far from our thoughts. Interestingly, Ted says he looks for what is different as he does his work; by contrast, I look for what is the same. In seminar situations it is predictable that he will identify and contrast the opposites whereas I will grope for a thread to connect the pieces together, as the paragraphs immediately above this one illustrate.

This dedicated neuropil idea has features to please us both. All neuropil samples are nothing more than extracellular fluid surrounded by neuron

and glial terminals, which means they can look alike to observers even at the electron microscope level. However, a neuropil sample such as the vomiting center in the medulla must have a very different organization from that of the respiratory center located nearby. Someone some day will surely find the way to measure these differences, and, if still around, I will congratulate Bullock for having been right all along. Vive la difference!

Acknowledgements

Selected Publications

Potentials from the body wall of the earthworm. *J Gen Psychol* 1939;20:339–348.

Characteristics of the loss of tension by smooth muscle during relaxation and following stretch. *J Cell and Comp Physiol* 1941a;17:85–95.

Cochlear potentials from the bat. *Science* 1941b;93:215.

(with Griffin DR) The sensory basis of obstacle avoidance by flying bats. *J Exp Zool* 1941;86:481–506.

(with Therman PO, Forbes A) Electric responses derived from the superior cervical ganglion with microelectrodes. *J Neurophysiol* 1941;3:191–200.

(with Griffin DR) Obstacle avoidance by flying bats: The cries of bats. *J Exp Zool* 1942;89:475–490.

The avoidance of obstacles by flying bats: Spallanzani's ideas (1794) and later theories. *Isis* 1942;34:132–140.

(with Morgan CT) Production of audiogenic seizures by tones of low frequency. *Am J Psychol* 1942;55:555–559.

Cochlear potentials elicited from bats by supersonic sounds. *J Acoust Soc Am* 1943a;14:41–49.

Flight in the dark: A study of bats. *Scientific Monthly* 1943b;56:155–162.

(with Morgan CT) Production of audiogenic seizures by interrupted tones. *J Exp Psychol* 1943;32:435–442.

(with Davis H) The response of single auditory nerve fibers to acoustic stimulation. *J Neurophysiol* 1943;6:39–58.

(with Davis H) Inhibition of activity in single auditory nerve fibers by acoustic stimulation. *J Neurophysiol* 1944;7:287–304.

(with Davis H) Action potentials from auditory-nerve fibers? *Science* 1948; 108:(2810):513.

(with Fenn WO, Otis AB, Rahn H) Corneo-retinal potentials in anoxia and acapnia. *J Appl Physiol* 1949;1:710–716.
(with Davis H, Morgan CT, Hawkins J, Smith FW) Temporary deafness following exposure to loud tones and noise. *Acta Otolaryngol* 1950;Suppl. 88:1–57.
(with Morgan CT, Garner WR) Pitch and intensity. *J Acoust Soc Am* 1951;23:658–663.
Suppression of auditory nerve activity by stimulation of efferent fibers to cochlea. *J Neurophysiol* 1956;19:424–437.
(with Hubel DH, Henson CO, Rupert A) "Attention" units in the auditory cortex. *Science* 1959;129:1279–1280.
(with Rose JE, Hughes JR) Microelectrode studies of the cochlear nuclei of the cat. *Bull J Hopkins Hosp* 1959;104:211–251.
(with Schwartzkopff J, Rupert A) Microelectrode study of superior olivary nuclei. *Am J Physiol* 1959;197:527–536.
(with Morgan CT) The neural basis of learning. In: Field J, Magoun H, Hall VE, eds. *Handbook of Physiology–Neurophysiology III*. Washington, D.C.: *Am Physiol Soc* 1960: 1471–1499.
(with Myers RE, Sheatz GC) Extralemniscal activation of auditory cortex in cats. *Am J Physiol* 1961;200:(1):23–28.
A glia-neural theory of brain function. *Proc Natl Acad Sci USA* 1961;47:129–136.
(with Pradhan SN) Some effects of anesthetics on the evoked responses in the auditory cortex of the cat. *J Pharmacol Exp Ther* 1963;139:97–106.
(with Manuelidis E, Fischer D, Chimienti J, Stein M) Observations on antibrain antibodies. *Science* 1966;152:673–674.
(with Norton T, Frommer G) Optic tract lesions sparing pattern vision in cats. *Exp Neurol* 1967;18:8–25.
(with Hillyard SA) Effects of stimulus and response contingencies on a surface negative slow potential shift in man. *Electroenceph Clin Neurophysiol* 1967;22:297–304.
(with Klivington K) Resistance shifts accompanying the evoked cortical response in cat. *Science* 1967;157:211–213.
(with Norton T, Frommer G) Optic tract lesions destroying pattern vision in cats. *Exp Neurol* 1967;18:26–37.
(with Petran M, Hadravsky M, Egger MD) Tandem-scanning reflected-light microscope. *J Opt Soc Am* 1968;58:661–664.
(with Kitahata L, Amakata Y) Effects of halothane upon auditory recovery functions in cats. *J Pharmacol Exp Ther* 1969;167:14–25.
The glia-neuronal interaction: some observations. *J Psychiatr Res* 1971;8:219–224.
(with Velluti R, Klivington K) Evoked resistance shifts in subcortical nuclei. *Curr Mod Biol* 1968;2:78–80.
(with Bauer J, Picton T, Squires K, Squires N) Loudness enhancement following contralateral stimulation. *J Acoust Soc Am* 1972;52:1127–1130.
(with Elmasian R, Bernheim A) Loudness enhancement and decrement in four paradigms. *J Acoust Soc Am* 1980;67:601–607.
(with Makeig S, Talmachoff P) A 40 Hz auditory potential recorded from the human scalp. *Proc Natl Acad Sci USA* 1981;78:(4):2643–2647.

(with Chou C-K, Guy AW) Auditory perception of radio-frequency electromagnetic fields. *J Acoust Soc Am* 1982;71:(6):1321–1334.

A Career Retrospective. In: Samson FE and Adelman G, eds. *The Neurosciences: Paths of Discovery II*. Boston: Birkhauser,1992a: 261–280.

A comparison of certain gamma band (40 Hz) brain rhythms in cat and man. In: Basar E and Bullock TH, eds. *Induced Rhythms in the Brain*. Boston: Birkhauser,1992b: 201–217.

(with Wilson M-J, Silva PD) Diagnosing hearing loss in the intensive care nursery: A 20-year summary. *J Am Acad Audiol* 1994;5:151–162.

(with Juhasz G, Kekesi AK, Nyitrai G, Szilagyi N) Natural sleep modifies the rat electroretinogram. *Proc Natl Acad Sci USA* 1994;91:5153–5157.

The 1939–40 experiments that validated Jurine's claim. *Le Rhinolophe* 1996;11: (Symposium Jurine) 17–25.

Epic X: Past, present, future. In: Karmos G, et al., eds. *Perspectives in Event-Related Potentials Research*. Amsterdam: Elsevier, 1995b: 1–20.

Additional Publications

Davis H. The Professional Memoirs of Hallowell Davis. St. Louis MO: The Central Institute for the Deaf, 1991.

Gardner H. Frames of mind: the theory of multiple intelligences. New York: Basic Books, 1983.

Gerard RW, Marshall WH, Saul, LJ. Electrical activity of the cat's brain. *Arch Neurol Psychiatry* 1936;36:675–735.

Gerard RW. The minute experiment and the large picture. In: Worden FC, Swazey JP, Adelman G, eds. *The Neurosciences: Paths of Discovery*. Cambridge MA: MIT Press,1975: 457–474.

Hyde IH. A micro-electrode and unicellular stimulation. *Biol Bull* 1921;40:130–133.

Jasper HH, Smirnov GD, eds. The Moscow Colloquium on Electroencephalography of Higher Nervous Activity. Montréal: *The EEG Journal* 1960.

Kelso JAS, Munhall KG. RH Stetson's Motor Phonetics: A Retrospective Edition. 1988: Boston: Little, Brown.

Mihailovic L, Jankovic BD. Effects of intraventricularly injected anti-N caudatus antibody on the electrical activity of the cat brain. *Nature* 1961;1962:665–666.

Morgan CT. Physiological Psychology. (1st ed.). New York: McGraw Hill,1943.

Morgan CT. Physiological Psychology. (3rd ed.). New York: McGraw Hill,1965.

Noyes A, Pierce GW. Apparatus for acoustic research in the supersonic frequency range. *J Acoust Soc Amer* 1938;9:205–211.

Prosser RA, et al. Serotonin and the mammalian circadian system: I. *In vitro* phase shifts by serotonergic agonists and antagonists. *J Biol Rhythms* 1993;8:(1):1–16.

Prosser RA, et al. A possible glial role in the mammalian circadian clock. *Brain Res* 1994;643:(1–2):296–301.

Renshaw B, Forbes A, Drury C. Electrical activity recorded with microelectrodes from the hippocampus. *Amer J Physiol* 1938;123:169–170.

Renshaw B, Forbes A, Morison BR. The activity of the isocortex and hippocampus: electrical studies with micro-electrodes. *J Neurophysiol* 1940;3:74–105.

Schmitt FO. The never-ceasing search. Philadelphia: American Philosophical Society, 1990.

Schreiner L, Kling A. Rhinencephalon and behavior. *Amer J Physiol* 1956; 181:486–490.

Strumwasser F. A circadian rhythm of activity and its endogenous origin in a neuron. *Fed Proc* 1963;22:220.

von Bekesy G. Experiments in hearing. (EG Wever, Trans.). (Acoustical Society of America ed.). New York: McGraw-Hill,1960.

Wickelgren WO. Effects of walking and flash stimulation on click-evoked responses in cats. *J Neurophysiol* 1968;31:(5):769–76.