The Early History of EPL
(The Eaton-Peabody Laboratory of Auditory Physiology)

Introduction:

What is the Eaton-Peabody Laboratory (EPL)? By some counts there are now more than 90 currently active EPLers. Since the mid 1950s it has existed in name but has never been a legal entity; there was no formal process to accept members, so for much of its first 40 years, as Director, I validated membership simply by treating individuals as members. There were no rigid rules as to what the prerogatives or obligations of membership were. This is the story of how this enigmatic group was conceived, started, and evolved into its present (circa 2008) form and what lessons its history may have for sociological studies of multidisciplinary laboratories.

After World War II, the United States of America fell in love with research and created many avenues of funding, both governmental and private. Medicine was an obvious direction that could benefit from this euphoric attitude. On May 21, 1956, the Massachusetts Eye and Ear Infirmary (MEEI) officially dedicated three floors for research. These floors were added on top of the existing "Connecting Building" that linked the Infirmary and the Massachusetts General Hospital (MGH). One of the socially prominent surgeons in Otolaryngology at the MEEI, Dr. Francis L. Weille[1], belonged to the St. Botolph Club, another member of which was Dr. James Killian, then the President of the Massachusetts Institute of Technology (MIT). Weille invited Killian to the dedication ceremonies but was taken aback by Killian's off-hand remark that "It is too bad that you don't have any real research here." Intrigued by this casual evaluation, Weille pressed Killian to elaborate and extracted a promise to see if MIT could help bring "science to the bedside."

[1] Dr. Weille graduated from the Harvard Medical School in 1925 where he studied with Dr. D. Harold Walker (class of 1898, Harvard Medical School) his future father-in-law. Dr. Walker was the LeCompte Professor of Otology at Harvard Medical School and the Mass. Eye and Ear Infirmary. His brother William was head of the Chemistry Department at MIT and the Walker Memorial Building there was named in his honor.

President Killian, obliged to make good his promise, examined the roster of MIT faculty and found one person who had done research on hearing. That was Walter A. Rosenblith, who had published some papers based on several years' work at the Harvard Psychoacoustics Laboratory under Professor Stanley Smith Stevens (Smitty). Walter, who held a degree of *Engenier Radio* from France, joined MIT's Electrical Engineering Department to start the Communications Biophysics Laboratory[2] in the Research Laboratory of Electronics (RLE). He had attracted the attention of Norbert Wiener, at that time, the most famous of MIT's professors, who was fascinated by the mathematical characteristics of electroencephalographic recordings ("brainwaves"). Rosenblith put together a group of young people with backgrounds in engineering and neurology (from the MGH) to apply computers to the study of the brain. A subsection of CBL worked on the auditory system and it was this crew that attracted Killian's attention, so he asked Walter to meet with the MEEI people.

Rosenblith chose not to meet with Weille and colleagues personally, but designated three people from the CBL to do so. Thus Lawrence Frishkopf (Larry), Robert M. Brown (Bob) and I, Nelson Yuan-sheng Kiang, went one evening in the fall of 1956 to the Infirmary to meet with Dr. Weille and his colleague, John W. Irwin, an internist at the Massachusetts General Hospital who ran the allergy unit there, together with Weille and Walter Burrage.

After Larry was introduced as a physicist, Bob as an electronics expert, and I as a neurophysiologist, Weille's first question was addressed to me. He asked, "I can see why we need a physicist and an electronics engineer, but why do we need you?" Presumably, he felt that Harvard had plenty of physiologists, so MIT did not have to supply one. I answered by saying that my doctoral research was done physically in the Ear, Nose, and Throat section of the Surgery Department at the University of Chicago, so I was, in some sense, acting as an interpreter. After describing the Infirmary and taking us on a tour of the facilities, Weille and Irwin explained what might be accomplished (still very vague). We three then parted and reported back to Walter. Larry and Bob expressed no interest

[2] Later changed to the Communications Biophysics Group when people realized that it would be confusing to have a "laboratory" within a laboratory.

in any further contact with the Infirmary, so Walter asked me to maintain contact with the Infirmary until we could write a report for President Killian.

Over the next few months through John Irwin, I met many otolaryngologists, none of whom knew anything about Weille's initiative. I had known Dr. Moses H. Lurie, the best known researcher in otolaryngology at the Infirmary, from his visits to Chicago, where his daughter Susan worked for Professor Ward Halsted in the Psychology Department.[3] What research was being done at the Infirmary at that time was mostly done by clinicians as labors of love, on their own time, with their clinical duties having top priority.

I wrote a brief report for Rosenblith but gave him a more detailed evaluation orally. The formal report suggested that a full-time researcher be hired, and to leave the future planning to this person. I included a list of the best mid-career auditory scientists who might be recruited. I do not know if Walter passed my recommendations on to President Killian, but after some time, John Irwin asked to see me about my recommendations. I remember meeting him at the Infirmary when he told me that a number of people in Otolaryngology, including the Chief, LeRoy Schall, had thought about my recommendations and the consensus was that they wanted me to take the position. I was genuinely surprised and said that my plan was to go the University of California Los Angeles (where Horace Magoun had offered me a position to study the physiological basis of consciousness) after learning a bit more about computers at MIT. John asked if I would be willing to help plan a laboratory since I would be in Boston for awhile anyway. I agreed to help but emphasized that I had published nothing and had no reputation as an expert in anything. Walter was not eager for me to leave the CBL as I was one of the more active members of the group, so an arrangement was made for me to remain a staff member of the Research Laboratory of Electronics with part of my duties to be an advisor to the MEEI otolaryngologists.

At that time I was engaged in a number of studies on the auditory system and was working with anyone in CBL interested in hearing. Through these projects I grew to know the aforementioned Bob Brown very well. He was a self-taught electronics tinkerer

[3] Later she married the animal caretaker in our (William Duwayne Neff's) laboratory, who eventually became a physics professor at Yale University.

who had come to MIT with Walter from the Psychoacoustics Laboratory at Harvard. He had graduated from Harvard with a degree in social relations. I asked him as a friend to help me advise the Infirmary which he agreed to do. Neither of us were paid for this work.

The Infirmary had installed a sound-treated room on the fourth floor of the connecting building in anticipation of future hearing research. It was being used by Dr. George Reed in tinnitus studies.[4] When Bob and I examined the room, we ran a few tests and decided that the construction was so fundamentally flawed that the room could not be modified to be usable as a sound-isolation chamber for auditory experiments requiring low background noise levels. We recommended starting over. By this time, Weille had elicited financial support for hearing research from Miss Amelia Peabody, a personal friend and MEEI Board member. He suggested that a small building could be placed in the open courtyard of the Infirmary. Irwin proposed that a grant could be submitted to the National Institutes of Health to fund research if MIT would agree to staff such a laboratory. Impressed by such enthusiasm, I agreed to oversee the project for however long I would be around but was still intending to join Magoun.

Up until then, the discussions had assumed that the new laboratory would start as part of Irwin's already established Microcirculatory Laboratory in the Infirmary, but as my interests were more broadly based than just the circulation to the ear, it was felt that a new name should be given the new enterprise. At that time there was no physical facility that was available for immediate exclusive use in auditory experiments so a new building was proposed. Because Miss Peabody had donated most of the funds for the new building, Weille thought that she should provide the name. She suggested that it be named the "Eaton Laboratory" in memory of her stepfather[5]. Weille persuaded her to add her family name and I suggested that the name should define its mission of studying the auditory system. Finally the name "Eaton-Peabody Laboratory of Auditory

[4] George had a not unreasonable idea that tonal tinnitus was produced by hyperactivity in frequency-specific regions of the cochlea and tried to alleviate the symptom by blasting the ear with high-intensity, frequency-specific tones in an effort to eliminate the abnormal activity.

[5] Mr. Eaton lived in the same building that housed Dr. Weille's office (247 Commonwealth) and was purportedly one of the founders of Ocean Spray.

Physiology" satisfied everyone and has continued to be its formal designation to this day although most people simply call it the Eaton-Peabody Laboratory. From the outset, the laboratory was conceived of as a multidisciplinary group of people from four institutions: The Massachusetts Institute of Technology, Harvard, Massachusetts General Hospital and the Massachusetts Eye and Ear Infirmary. For this arrangement to work, no one of these institutions would have ascendancy over the others. Thus the EPL was really an idea rather than a legal entity. Its legitimacy was entirely dependent on the institutional affiliations of its people. Membership was based on acceptance by other members.

The Basement Years

The planning of the courtyard building was done by Bob Brown and me (again without compensation) working with the architectural firm of Shepley, Bullfinch, Richardson and Abbot. The Infirmary had a longstanding relationship with this old Boston firm, especially through Henry Hixon Meyer, the Chairman of the Board of Trustees for the Infirmary, who was a highly respected Boston real estate attorney. The overall manager for the firm was Solon Bailey and the architect we dealt with mainly was Jack Peirce.

A primary consideration was to keep uncontrolled sounds from entering the experimental chambers which would complicate study of responses of the auditory system to acoustic stimuli. Neither Bob nor I had designed a building from scratch before and the architects had never designed a "vibration-isolated, sound-proofed, electrically-shielded" room before. So we were all learning from one another. We were fortunate to have a ground level space to work in, but the courtyard could be entered only through a narrow archway, so all heavy equipment (such as pile drivers) had to be brought to the site by dropping them in by a tall crane. Soil samples indicated that the extent of the filled land was too deep for us to drive piles that reached bedrock so we settled for "floating piles", driven sonically to minimize disturbances to all our surrounding neighbors. We designed a double-walled chamber, part of which was essentially a small room physically separated from but encapsulated by the rest of the new building. In the middle of the chamber was set an 800 lb. machinists' table that could be hydraulically moved up or down and rotatable. The table legs were set on bridge-bearing pads, acting as vibration isolators, which in turn rested on a heavy concrete slab that had three separate piles driven solely to support the table. The outer walls of the chamber were part of the rest of the building. The inner wall rested on a concrete slab separate from the table slab and the rest of the building. Both the inner and outer walls were covered with galvanized mesh tied together and connected to a large metal spike driven into the ground, thus forming a double Faraday Cage with a single ground. All connections between the outside and inside of the chamber had to go through specially shielded "penetration boxes", one on the outer wall and one on the inner wall,

so that hydraulic tubing and electric wiring introduced minimal acoustic or electrical noise. Ventilation and temperature control of the chamber was achieved through long "aircoustats" that minimized sounds entering the chamber through the air handling ducts. Lighting in the chamber was DC so as to avoid contamination of electrical signals from the outside. The entire EPL building had a total of 12,000 sq. ft. of usable space. In addition to the chamber there was a control room for equipment used to supply stimuli and process response data, an aseptic surgery room, an electronics-mechanical shop, and a multipurpose room used for data analyses, electrode making, meetings, office functions, etc. A small room with a toilet and sink was an essential component because some of the experiments lasted for many days.

There were several essential functions that could not be accommodated in the courtyard space. Among these were a place to accommodate animals including before and after chronic surgery and a histology/anatomy facility. These were functions that could be shared with the Microcirculatory Laboratory, so they were installed on the 6th floor of the Connecting Building where the Microcirculatory Laboratory under Dr. Irwin and the Otopathology Laboratory under Dr. Lurie had space.

Much detailed planning had to be done in order to cram all the necessary functions into a small space and within a limited building budget ($50,000 plus matching funds from the National Institutes of Health (NIH), courtesy of the Hill-Burton Act.) The actual construction of the building by Conti (the firm chosen by the Infirmary) required either Bob Brown or me to be present at all times as the standard procedures familiar to the workmen tended to be more casual than was needed to guarantee the integrity of the chamber. The most expensive piece of equipment was the large industrial air conditioning unit which had intricate controls to serve both the special needs of the chamber (requiring rapid control of temperature without introducing sound or vibrations) and the rest of the laboratory. Fortunately, John Irwin's father-in-law was the President of International General Electric at the time so a $50,000 unit was donated to the Infirmary for our use and was incorporated into the design of the building.

During the planning and building phase, I continued to conduct regular experiments at the Communications Biophysics Laboratory, often late at night. At that time, Walter was very busy at higher levels of MIT and was rarely (perhaps never)

involved in bench research. With my background in mathematics and physics, I was enjoying learning signal and systems theory from my electrical engineering colleagues. The administrators in the Research Laboratory of Electronics considered entries in the "Quarterly Progress Reports" to be publications, so I started to submit reports. In those days concepts such as peer-reviewed journal were not so important and the number of appropriate journals was small. Once I started submitting papers to journals, I would list both Research Laboratory of Electronics and the Massachusetts Eye and Ear Infirmary as my affiliations, even though the actual experiments were done in the Communications Biophysics Laboratory. By the time the new building was ready to be occupied, I felt committed to seeing the Eaton-Peabody Laboratory established on a firm footing. Putting equipment together was no simple task, as most of what we needed was not commercially available at that time. I had proposed in an application to the National Institutes of Health to put my background in surgery, physiology and information theory together in studying single neuron activity in the auditory system. In those days, NIH had so much money that there were hardly enough investigators to absorb it, so almost any reasonable proposal would be funded. This was before "grade inflation" so our first application, with a priority score in the mid-three hundreds, was funded at a level that was considered large at the time.

Because we had been frugal in using Miss Peabody's donation, we were able to pay a third of Bob Brown's salary to design and build the stimulus-generating equipment. Some of the recording equipment was bought and some built. We needed a full-time engineer and a research assistant to assemble a working laboratory while I was spending much of my time in the Communications Biophysics Laboratory doing experiments. After trying a few others, we finally hired Alan Crist, who had both electronics experience and machining skills to put mechanical, acoustical, and micromanipulator systems together. John Irwin and I had developed a system of recruiting graduates from Smith College and Mount Holyoke College to work as research assistants in the Microcirculatory Laboratory. He knew President Thomas Mendenhall of Smith and I had a friend and former classmate, Curtis Smith, who was a physiology professor at Mount Holyoke. Each spring we would travel to western Massachusetts and spend one day at Smith and one at Mount Holyoke where lists of job applicants had been prepared by the

respective placement offices. In the mid-fifties, many of the best research universities accepted only a few women graduate students, so some of the best graduates from women's colleges were interested in working in a scientific environment as laboratory assistants, either to decide on future careers or until they married. Indeed, we always found many more qualified candidates than there were positions to fill. One of the women hired by Irwin was assigned to work with me because she had been a physics major at Smith College. Louise Clark (later Smith) impressed us with her calm and steady personality as well as having patrician social skills (she was a direct descendant of Governor John Winthrop of Massachusetts). Our little laboratory was close to the cafeteria which was in the basement, so the researchers on the 4th and 5th floors of the Connecting Building would often drop in on their way to lunch to see how things were progressing. There was one more need; we had no secretary. Irwin had solved the problem for his laboratory by farming out his secretarial tasks to a woman, Gertrude Roberts, who worked from her home in Newton because she had seven children. Every now and then we would drive to her house, deliver our materials, and either wait for typed versions or leave it if the job was large (e.g. a grant application or progress report). This somewhat cumbersome arrangement was a holdover from when Mrs. Roberts worked for the Allergy Unit at the MGH.

So finally we had a skeleton crew where all the essential functions could be covered. As the various people got to know one another, we developed a surer sense of our individual competencies and proclivities. At the bench level, there was so much detailed work that had to be done that daily priorities were usually determined by immediate needs. At a different level, John and I would have discussions about day to day matters but also about long-term goals. John was just beginning to see how differently scientists, engineers and clinicians thought professionally. He had always intellectually appreciated the potential benefits but watching it unfold at a personal level was interesting. He and Walter Rosenblith were different in so many ways that they dealt with each other warily but open-mindedly, almost as if they were diplomats from countries that differed greatly in culture and interests. I found myself often acting as a translator. In any case, all of us were moving full-steam ahead as the facility gradually became more and more usable for experimental work. The first real experiments were

done in late 1958 and there was considerable excitement as results began to trickle in. Meanwhile, I had given several talks to groups such otolaryngologists, ophthalmologists, residents, nurses, medical students, administrators and trustees of both the Infirmary and the Massachusetts General Hospital. It soon became obvious to me that a basic science ethos was foreign to an environment where helping sick people was the main defining mission. At the same time, there was a general feeling that something new was being added to the hospital culture. Because the Infirmary is a teaching hospital of the Harvard Medical School, I was given an appointment at the Medical School, the significance of which grew in time. Our connection with the MGH was through John Irwin and later me.

In the first few years of MEEI and CBL collaboration, the experimental facilities at the EPL did not permit work that required carefully-controlled sounds. In addition, I had to work out the practical difficulties of single-unit recordings. The fact that Bob Brown's main job was at CBL significantly limited the time he was able to devote to building the stimulus-generating equipment promised. The equipment came in dribs and drabs. (E.g.: There was a long interval when the only signal generators available were pulses, thus accounting for the exclusive use of clicks in early experiments done at EPL.)

Given the close relationship with John Irwin, it is not surprising that early experiments at EPL involved making static pressure measurements and blood supply to the inner ear in various compartments of the cochlea. His earlier microcirculatory studies had demonstrated arteriovenous anastomoses in blood vessels in the stria vascularis. Some of these studies continued in the new EPL with the addition of electrophysiological measurements.

In the late '50s I divided my time between CBL and EPL in the following way. Projects that required computational facilities would be done largely at MIT. Projects that required sterile animal surgery or histological analyses would be done at EPL. Thus a series of papers issued from CBL that exploited signal averaging techniques to break new ground in auditory physiology. Meanwhile, at the Infirmary we explored techniques of recording electrical responses in awake cats with chronically-implanted gross electrodes. One series involved a half dozen animals with electrodes on the round window, "primary auditory cortex" (AI), "secondary Auditory cortex" (AII) and frontal cortex (originally thought of as a control location). Not unexpectedly, there was

enormous variability in responses to clicks (the only stimuli we could generate) as the animals were free to roam about and even when they were at rest. Our reference electrode was usually on the occiput and there was often quite a bit of muscle activity recordeds. The round window electrode usually showed lots of irregular activity that we attributed to middle-ear muscles as they did not appear in the other leads. There were many surprises (e.g. some of the largest click-evoked responses were from the frontal electrodes. In any case, there would have to be many methodological improvements to control behavior, state, and acoustic stimuli to continue this line of experiments so we terminated them. Similarly, a series of experiments was started by our first Otolaryngology fellow, Floyd Goffin, on the effects on cochlear responses of perfusing the cochlear scali with various pharmacological agents. These were again filled with intriguing results but Floyd had only a year to spend in research and this was too short to run all the necessary control experiments needed to justify publication.

Our signal averaging experiments on evoked responses had significant impact. We were visited by many colleagues anxious to use the new computer methods for their own studies. My old friend Samuel Sutton from Chicago days came up and spent time learning the techniques which he applied to later components such as the P-300 responses. His work at the Psychiatric Institute in New York became well-known. Hallowell Davis at the Central Institute for the Deaf regularly visited us and became an enthusiastic advocate of signal averaging methods. Jerzy Rose invited me to Johns Hopkins to describe our methods and later introduced them to the University of Wisconsin when he moved there.

Some of the postdoctoral fellows in CBL were attracted by the new opportunities in EPL and collaborated with me on a number of studies that were highly successful. Donald C. Teas and I explored the effects of "state" on cortical evoked responses. George Gerstein and I developed methods of displaying single-unit results. In another series, we prepared chronic animals such as those with cut auditory nerves. After allowing many weeks for spiral gangion cells to degenerate, Bill Peake and I could study cochlear responses without contamination by neural responses. The histology of these ears would later lead to other lines of experiments. Working with Walter's graduate students and fellows was particularly productive, both in terms of scientific discoveries

and in establishing long-lasting friendships. Both Moise Goldstein and Bill Peake, the first two graduate students I worked with, became pioneers in bringing computer processing of data into auditory physiology. When William Talbot was starting bioengineering at Johns Hopkins, he came up to consult with Walter and me about recruiting young faculty members for his new department. I suggested Moise who did go to Hopkins, where he continued to be interested in the auditory cortex. After getting his Sc.D., Bill Peake joined the Electrical Engineering Department as an assistant professor, so we continued our collaborations and eventually he did most of his experimental work at the Infirmary.

During this time I was steadily improving the infrastructure for single-unit studies. One by one, pesky problems were solved. A hydraulic micromanipulator system enabled us to move electrodes in one dimension remotely from the control room. Jerry Letvin's group at MIT had devised a two-stage glass micropipette puller which we found useful. We tried virtually all the known kinds of electrodes. The surgical exposures to the auditory nerve and cochlear nucleus in the cat were developed during the denervation experiments. The use of Dial-urethane as an hypnotic-anesthetic agent for long-lasting experiments proved satisfactory for long-lasting single-unit studies.

With all of these activities progressing well, we had no problems with renewing our NIH grant. In those days, almost every proposal was examined in depth by a site-visiting inspection team that reported back to the study section. Our priority scores were soon receiving the highest possible scores and we got to meet many of the best-known people in the field. In keeping with our avowed mission, Weille and Irwin insisted that I report our results at Otology meetings and publish in their journals. This was not only good advice for "political purposes", but I also learned how to communicate basic scientific results to clinicians. This skill was honed in my regular teaching sessions to otolaryngology residents at the Infirmary. One outcome was to convince people that signal averaging techniques could be used to distinguish between problems arising in the ear from problems arising in the brain. Eventually, this test has become mandatory in most states for infants and has been established as standard in most developed countries.

Although working with postdoctoral fellows was very productive, the opportunity to work with graduate students was in some sense even more gratifying. When Walter

Rosenblith moved on to higher administrative positions, CBL was led by William Siebert, a radar engineer from Lincoln Laboratories, who had joined CBL as a much-needed theoretician. He and I got along well and eventually we found our work complemented one another's in that his theoretical ideas were based on my experimental data. Bill Peake and I began to teach a graduate course in Electrical Engineering, "Signal Processing in the Auditory System" which brought many students into CBL and EPL. Bill became the principal "recruiter" of such students after Moise left for Hopkins (bequeathing his graduate student, Murray Sachs, to EPL.) One of the earliest such students was John Guinan, who started working with Bill on measuring the motion of the stapes in cats using stroboscopic illumination. So much was going on that one experimental chamber was no longer sufficient, so we planned an addition to the laboratory as I was writing "The Monograph" on "Single Unit Discharges of the Cat's Auditory Nerve". We were able to raise the funds and worked again with Jack Pierce who had by then started his own architectural firm. The new addition doubling our space was officially dedicated in 1966. Howard Johnson led the ceremony as his first official act after assuming the Presidency of MIT. John Irwin and I carefully chose the dedication invitees with Walter's help. I remember the occasion well, as tea was served in the laboratory and I had a chance to meet the Governor of Rhode Island, John Chafee; the Director of the National Institute of Neurological Diseases and Blindness at NIH, Richard Masland; and many important people from MIT, the Harvard Medical School and the Massachusetts General Hospital. A number of Infirmary trustees attended, including, of course, Amelia Peabody, who seemed extremely pleased.

After most of the guests had left, Peter Elias, the Head of the Electrical Engineering Department at MIT, stayed for several hours. It seemed that Bill Peake was under consideration for promotion and Peter wanted to hear more about the collaborations that had developed between his department and EPL. I described, not only our ongoing research, but also what we foresaw in studying the neural bases for auditory communication. I emphasized the contributions of engineers to communication sciences (Peter was an expert in Information Theory). This was mainstream engineering and an important branch of electrical engineering. Both speech and hearing research had received major inputs from engineering and the results impacted society in many ways.

At that time the patent for the telephone was thought to be the most valuable patent in history. As Peter left, he remarked that the important link between EPL and MIT was apparent and he appreciated the key role that Bill played. Soon thereafter Bill became tenured, thus ensuring that EPL's source of students from MIT would be secure for the foreseeable future and Bill's knowledge and advice would be available for such students.

The Harvard Medical School Unit

Once the Eaton-Peabody Laboratory's scientific reputation had been established and the linkage between MIT and the MEEI had been firmly established, John Irwin and I began to think about our relationship with the Harvard Medical School. The Department of Otology and Laryngology at Harvard was generally regarded as a clinical department with little interaction with the basic-sciences departments, which were mostly located in the Longwood Medical Area. I had been given an appointment in the Physiology Department but not much teaching was asked of me and there were few people in that department who worked on hearing despite its historical record of interest before World War II. While our physiological experiments were going well, we had an acute need for more anatomical knowledge of the regions of the brain that we were studying (in particular, the cochlear nucleus and its projections). Much of the existing literature on the cochlear nucleus was old and difficult to relate exactly to our single-unit studies. Bruce Warr had come to us from Mike Harrison's laboratory at Boston University to do brainstem anatomy, but was mainly a psychologist by training. John and I met with Don Fawcett[6], the Chairman of the Anatomy Department at the Harvard Medical School who felt that collaboration between his department and the Eaton-Peabody Laboratory would be a good joint project. He agreed to provide the space and a junior faculty appointment in Anatomy if EPL would find the person, provide the salary, and equip the laboratory.

I had known Grant Rasmussen when he was at the University of Buffalo, but he then moved to NIH to start the Laboratory of Neuroanatomy under William Windle. I visited him to ask his advice about promising young neuroanatomists. He had two fellows working with him at that time, Richard (Dick) Gacek and D. Kent Morest, both studying the auditory system. Dick was scheduled to come to the Mass. Eye and Ear Infirmary as a resident in Otolaryngology, but Kent wanted to make his career in anatomy. Kent had gone to the University of Chicago as a medical student and was considering returning to be in their anatomy department. His special focus was reviving

[6] Don was a histologist whom I knew because he had taken over the authorship of the standard histology textbook, which started as a University of Chicago text by Maximov, then became Maximov and Bloom (William Bloom was my histology professor at Chicago), then Bloom and Fawcett, then Fawcett.

the Golgi method to study neurons in the auditory brainstem – just what we needed. Grant gave his blessing and Kent came to Harvard.

During that time, a series of papers on the anatomy of the cat cochlear nucleus emerged from Norway, by a young woman, Kirsten Osen. Her work and Kent's gave physiologists the basic data we needed to interpret our results and many papers ensued forthwith. The basic question we sought to answer was: Could one predict the input-output functions (physiological characteristics) of neurons if one knew the morphology of the neurons and the anatomical characteristics of the endings on those neurons. By analogy, in those days, one could guess the input-output functions of an electronic component (resisters, capacitors, inductors, etc.) by looking at its shape. Similarly, if one could gather sufficient anatomical knowledge, one might be able to predict the functional characteristics of neurons. Eventually, by combining such knowledge with knowledge of the connectivity of the neurons, an appreciation of the functional significance of specific networks might be gained.

After a dozen years, Kent left for the University of Connecticut and one of his postdoctoral fellows, Nell Cant, took over the anatomy laboratory, but she left shortly thereafter to return to North Carolina for personal reasons. Meanwhile, David Ryugo had taken a teaching position at the University of Vermont. I visited him there and was impressed by his energy and willingness to learn. With the support of Elizabeth Hay (then the Chairperson of Anatomy) he was appointed as an assistant professor of anatomy at the Harvard Medical School. Thus the anatomical arm of EPL was re-established. For a number of years the combination of physiology and anatomy continued to prosper. An interesting observation is the difference between the attitudes of people at the Infirmary and those of the Medical School people, a topic that will be explored in a later section.

Interacting with the sociology of the laboratory is the ever-changing funding mechanisms of NIH (as emphasis shifts from small individual-investigator grants to large program project or center grants and back again or from basic inquiry to disease-relevant research). It is important to keep track of changing moods which are heavily influenced by general economic conditions. A relatively large laboratory such as EPL has to be flexible enough to reorganize quickly without losing sight of its scientific focus.

Especially important is the ability to retain a trained technical force during all the ups and downs of funding. Not only is such a crew indispensable for continuity of effort but it needs always to improve and take advantage of technological advances. One of the most interesting stories is how the division of duties in EPL shifted and adjusted over the decades. Meanwhile, we return to a description of the MEEI base for EPL activities.

The Carleton Street Years

After the second Chamber in the basement lab was activated, scientific progress moved ahead rapidly and our NIH grant applications were always funded. By the late sixties, it became increasingly obvious that the clinical facilities of the Infirmary were hopelessly out of date. The trustees decided on a major construction project to expand and modernize the hospital. Many possible plans were examined but because the only land available was the courtyard where our one-story building sat, we were asked to move to new space in the Charles Street Garage next to the "Nurses Residence". However, it eventually proved too difficult to persuade the Beacon Hill Architectural Commission to allow a wet biological laboratory on Charles Street. A parade of architects, some of them famous (e.g. Hugh Stubbins), were consulted, but eventually a firm, Walk Jones, from Memphis, was given the job to build a new hospital over the existing one, as it was impossible to consider shutting down the hospital for a few years. The chief architect was a Chinese-American named Francis Mah who had been a classmate of Walk Jones Jr. He was considered the brightest architect in the firm so in order to keep him, the firm's name was changed to "Walk Jones, Mah and Jones."

During the negotiations, we were informed that our laboratory would have to be demolished to erect the new building, but that EPL could have space in the new building provided we could raise the money for the space, since the campaign to raise building funds would not include us, despite the fact that our research was heavily touted in the campaign. John Irwin was disgusted with this decision, as was Hal Schuknecht, who wrote the trustees a powerfully worded letter about the importance of the EPL to the future of the Infirmary. Eventually, the Infirmary trustees voted to reimburse the cost of building both basement sections of the EPL, which monies could be used in any way we saw fit. With more than half a million dollars guaranteed, we examined our choices.

First, Schuknecht, Irwin, Weille, and I decided that the original mission of the EPL to "bring basic sciences to the bedside" had proven to be feasible and even more promising than when the idea first appeared. Second, we decided to ask Miss Peabody to help fund space in the new building for EPL. Dr. Irwin felt that it might still be possible to get NIH matching funds, even though the Hill-Burton act was being phased out and was unlikely to be renewed. Finally, I was to examine all possible ways to continue our

research as obligated by our acceptance of NIH research grants, while the new building was built with EPL space included.

I had accumulated enough data and figures for a second monograph on auditory-nerve activity in cats but had to shelve working on the manuscript in order to deal with the space problem. We had to have space equivalent to our existing space, as we were already bursting at the seams. This space had to be ready within months as the EPL building was scheduled for demolition in order to construct the new hospital. Thus, simultaneously we had to plan for space in the new hospital building and find the funds to pay for it as well as find a way to keep our research going during the years of construction. Our research had to proceed uninterrupted until the last possible moment if progress on our grants was to be uncompromised. The next few months were incredibly packed with decisions large and small, made virtually every moment. I looked into renting space commercially, and in the Schepens Eye Institute, which had some empty space (but not enough) and the Massachusetts General Hospital. By good fortune, an MIT-owned building on Carleton Street in Cambridge was temporarily unoccupied, which was just the right size. Our half million dollars would pay for installing two "soundproofed" chambers and ancillary facilities. The indirect costs from our grants could cover the rent from MIT. We had to use our connections with Walter Rosenblith, by now Provost at MIT (whose duties included chairing the Space Committee) to negotiate animal care and disposal facilities as well as parking spaces. I discovered that one of the most powerful persons at MIT was John Wynne (one of the vice presidents) who was in charge of assigning parking space. Conveniently, there was an empty lot across Carleton Street which was waiting for adjoining properties to be acquired by MIT before a new building could be built on it. There seemed to be some problems in obtaining the needed lots so we were granted permission to use the empty lot for our parking until all issues were settled. It was just the right size and we were not asked for rent. I had checked the E-42 building and because it was old, the loading limit had a safety factor many times what modern buildings had, so we were able to buy and install two heavy acoustical chambers in less than a month after first installing I beams to vibration-isolate the chambers. Miraculously, everything fell into place and during the time it took for the equipment to be installed and the surgery and histology space to be

equipped, we had temporary quarters in the Nurses Residence which fortuitously had been largely vacated by the nurses who could now afford to rent more desirable living quarters.

Although it was a hectic time, there was a certain pleasure in solving dozens of practical problems each day. Everyone in the laboratory performed beautifully in scheduling experiments so that our down time could be used in writing up papers or analyzing results. From the outside, it seemed as if nothing disturbed the scientific work. It was gratifying that in times of stress the EPL team pulled together and morale was high. In fact, people found it exhilarating to overcome each difficulty as it arose.

A side benefit for those of us who taught classes at MIT was that we no longer had to cross the Charles River to go from classrooms to research laboratory. A liability was that we were now separated from the clinicians with whom we had begun to really bond. I made it a point to participate in as many hospital functions as I could, to maintain a psychological presence. Teaching basic sciences to residents and fellows continure to be done.

Altogether, we sent 3 ½ years at MIT, during which time we were able to raise the funds necessary to build a new enlarged laboratory facility with four chambers, control rooms, and space for surgery, histology, computers, and engineering functions and even room for an office, library and data analysis.

The planning of the EPL space in the new hospital building was complex after we rejected the basement because it would be below the water table. Because the outer walls of the basement would be vulnerable to cracks and subsequent leaking of water, mujltiple walled chambers would not allow access to repair cracks in the outer walls. Thus we had to opt for a higher floor which created a load bearing problem. We hired an acoustical engineer from Bolt, Beranek and Newman, Dr. Istvan Ver, to work with Bob Brown and me in designing the knew chambers. We estimated the weight of these chambers to be 80 tons apiece so they had to be placed apart from one another to distribute the weight evenly. We also had to worry about who would be our immediate neighbors in 3 dimensions so that we could minimize electrical or magnetic interference. The details of

the chambers are described elsewhere[7], but when they were being constructed, either Bob Brown or I had to be present at all times. For example, the construction crew from Conti (Phil) was accustomed to putting excess grout into any convenient place that would be enclosed such as the spaces between the walls of the chamber. This of course would ruin the mechanical isolation of the chamber walls and would be hard to detect. Similarly, it was all too easy to break the electrical shielding or to connect it improperly.

During the construction, we became friendly with all members of the building trade, from the architects, the systems designers, the engineers, the construction crew, and the specialists such as plumbers, carpenters, electricians, lighting experts, heating and ventilation, etc. Surprisingly, my background in embryology helped me to understand the importance of timing in construction. Just as genes are activated at specific times by specific agents, the various specialties are scheduled to appear and do their work in an elaborate sequence that is meticulously planned and organized by the general contractor. Each specialist also has to fit his own schedule to the needs of other job sites. One can see how working with subcontractors who are familiar, honest, skillful, reliable, cooperative, and cordial is an essential component of any smooth progress in any building enterprise. The web of trust is woven by a complex mix of individuals. All these factors have to be considered when a contractor bids on a job. Far from being a chore, the intellectual involvement in constructing a physical building taught me much about how to build a functioning laboratory[8]. I used the experience later in helping the Children's Hospital build their audiological facilities.

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[7] Vér IL, Brown RM, Kiang NYS. Low-noise chambers for auditory research. J Acoust Soc Am. 1975; 58:392-398.

[8] The development of a normal auditory system also depends upon the orderly supply of materials at the correct times. The number of genes known to be involved in hearing increases as more studies become available. Disruptions in when specific genes are turned on or off will lead to altered hearing, usually as defects, although sometimes as improved modifications. Anyone who has participated in putting a modern building together is equipped to think about genetic disorders of hearing and the evolution of specific hearing mechanisms. In fact, we had to build a new hospital without fatally interrupting the operations of the old hospital, perhaps an extreme case of remodeling. In

Bob Brown was not so enchanted with the educational aspects of this activity. Indeed the stress of monitoring the construction became intolerable for someone with a "loner" disposition, so he resigned his job despite all adjustments intended to relieve the pressure. Thus, I had to drop most of my scientific work to spend full time at the construction site. This was essential because every change order carried an increased expense and our budget did not carry much contingency funding. One of my greatest personal satisfactions was that there were virtually no change orders initiated by us, so that we were able to bring the project to a close without extra expense for which the administration would have held us responsible.

A good example was the lighting. From my previous experience I had some idea of the prices for purchasing and installing the general lighting for a laboratory. When I went over the estimates, I found an order of magnitude greater figure than expected, so I made my own inquiries. It turned out that instead of using standard fixtures, special ones of unusual design were specified, which could not be justified by any functional reason that I could discern, even after discussing it with every person in the chain who had input into deciding on the lighting fixtures. I asked that our floor be fitted with standard fixtures, which would save us more than $100,000 (in 1970 dollars). Furthermore, I notified the Administration that if they did the same for the rest of the hospital, they could save more than a million dollars. To my surprise, I was told to stay out of the design for the other floors, which I did. I suspect that since the architects were paid a percentage of the total cost, there was no incentive to hold the expenses down and kickbacks are not unknown in the industry.

The greatest fear for everyone involved in the building was the spectre of strikes. At various points there was talk of strike possibilities (e.g. of carpenters) or some other

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the developing ear and brain there is also the issue of how to change structures smoothly while maintaining a functioning system. Similar ideas illuminate the understanding of how vertebrate ears and brains evolved and adapt to diverse ecological niches. By these cursory remarks I hope it is abundantly clear that we are nowhere close to understanding how we hear and how our present hearing apparatus evolved, presumably through mechanisms that left a trail which we can use to reconstruct the paths taken.

unforeseen difficulty in obtaining proper supplies or workers at the scheduled times. It is self evident that any disruption in scheduling would have ripple effects for everyone else. For the most part, there was a strong desire by everyone to keep progress moving smoothly and avoid disruptions that would create headaches for everyone.

The Fourth Floor Years

Eventually, in 1974, the fourth floor space in phase 1 of the MEEI "new" building was declared finished and it was time to move EPL back. By this time, many of the MIT people had found the Carleton Street quarters so convenient to RLE and the classrooms at MIT that there was a movement to retain the Carleton St. laboratory. This option would have split the laboratory but had some advantages. Three factors convinced everyone that this option should not be exercised. One, the new quarters at the Infirmary more than doubled our previous space so issues of crowding did not exist. Second, the number of grants would have had to be increased significantly to cover the overhead in both places. Thirdly, MIT had plans for the Carleton Street space and were glad to have us occupy the third floor usefully while they developed their original ideas. Finally, the basic idea behind placing a scientific laboratory in a clinical environment still held.

Because our research was in a particularly active period, the main principle we adopted was to minimize interruptions to the experimental schedule. We divided the entire staff into groups, each responsible for bringing the new facilities into operation for their own experiments. Thus, the equipment used by each group would be packed in such ways as to make reassembly almost automatic. We hired a moving company that specialized in moving sensitive and fragile equipment such as computers. In the end, everything was moved and reassembled in one day so that within a week, we were fully operational. One might think that having doubled the total space including the number of "sound-proofed" chambers, we would rattle around a bit in our new quarters, but like a gas we simply expanded to fill the space comfortably. Perhaps this was because we had been more cramped than we realized.

As we took on more projects, fortuitously NIH (in particular the Neurological Institute) introduced Program Project grants in order to encourage interdisciplinary research. This funding mechanism enabled us to attack problems such as acoustic reflexes explicitly rather than implicitly. Perhaps this is the place to note one of the benefits of a multidisciplinary effort: its multifaceted character. Every now and then funding agencies like to encourage certain forms of organizing scientific work. They will then emphasize "new" initiatives (e.g.: large program-project grants, center grants, core grants vs. small individual investigator grants.) In addition, from time to time there will

be a push to emphasize certain disciplines (e.g.: engineering, molecular biology, physiology, developmental biology, clinical research, etc.) Being inherently multidisciplinary, EPL could turn the momentarily most favored face to be the most visible aspect regardless of what was currently fashionable. Meanwhile as NIH and NSF would change their philosophies and personnel as time went on, it became important to keep track of what was happening politically on the national scene in order to predict the twists and turns in funding priorities.

To give only one example of how important it was to track national events, the double-digit inflationary years under the Carter administration created real problems for EPL. We had been very productive in the preceding years and our grants were being approved for 5 years with high priority scores. However, since the government's budget is approved yearly, we had to submit a budget each year which was limited to the amounts approved at the beginning of the 5 year period. One could ask for supplemental increases if there were very special unforeseen needs but an overall financial squeeze that affected everyone was not a sufficient reason for requesting a supplement, as everyone was subjected to the same conditions. Towards the last few years of our grant the inflationary spiral hit us hard especially because most of our budget was for salaries. We fell behind the salary scales at all our institutions so I began to pay more attention to establishing a safety net by obtaining endowment funds and working with the Infirmary trustees to promote greater understanding of the importance of basic research to the future of the Infirmary.

Meanwhile the research and teaching functions of the laboratory broadened as investigators began to obtain funding through R01 grants to support research focused on their individual interests so that the organization of the laboratory changed to reflect this "decentralization". As older colleagues retired, they bequeathed their space and funds to the EPL because they knew their resources would be used productively. These friends included Moses Lurie, Francis Weille, John Irwin, and William Montgomery. By the time I began to think about retirement in the late 80's, the research was prospering but our teaching had become endangered because the academic entities through which we taught were reorganizing. At the Harvard Medical School, the traditional departments of Anatomy and Physiology were gradually seen as archaic and descriptors such as

"cellular" and "molecular" were being introduced everywhere. More power was moving towards the principal investigators of large research or training grants. After the Anatomy and Physiology departments were replaced by more "modern" multidisciplinary departments. At the same time, the leadership of the MIT Electrical Engineering and Computer Sciences Department continute to downplay communication as a priority area so our faculty in "Area 7" would gradually atrophy through retirement. Thus our traditional base for recruiting students for EPL would, in the long run, be threatened at all levels. Clearly this situation had to be addressed.

I gathered a group of Harvard and MIT faculty interested in Speech or Hearing and proposed the formation of a Speech and Hearing Sciences Program that would provide an academic home for faculty and students interested in the hearing and speech communication sciences. This is not the place to describe the tactical steps that eventually led to the entity now known as the "Speech and Hearing Biosciences and Technology" program in the Harvard-MIT Division of Health Sciences and Technology. Suffice it to say that along the way we had to help create a new Institute for Deafness and Other Communicative Disorders at NIH in order to obtain training funds. This new SHBT program did not displace any existing programs but was added to supplement the older tracks that were anticipated to downsize over time.

The first class in the "Speech and hearing Sciences Program" entered in 1992 with seven students, most of whom subsequently spent some time at the MEEI and many of whom are still affiliated with the Infirmary. In 1996 I surveyed the formal institutional ties of the EPL and decided that the time was right to retire. This decision was based on the following.

1. The research base was strong, funded and well-regarded by the scientific community.
2. The trustees of the MEEI fully recognized the value of the EPL to the Infirmary and were willing to guarantee a professorship tied to leading the Laboratory.
3. The success of the Speech and hearing Sciences program (soon to be renamed the SHBT) provided a secure source of graduate students, supplemented by more traditional sources.

4. A nucleus of associate and full professors at MIT and Harvard provided an interconnected community of auditory scientists, all committed to working together. Almost half of these scientists were EPL members.

5. Under the leadership of Joseph B. Nadol Jr., the Chairman of the Otology and Laryngology Department at Harvard and Chief of Otolaryngology at the MEEI, there was a cadre of academic clinicians who had worked with the scientists in EPL and RLE so that a unique cultural relationship had been firmly established between clinicians and basic scientists.

6. The Research Laboratory of Electronics was how headed by John Allen who had once been a graduate student in CBL. He was a strong supporter of EPL.

7. M. Charles Liberman had been the Associate Director of EPL for several years and had proven his interest and capability to run the laboratory as an acting director and internal candidate to be my successor as director.

8. The leadership in HST had accepted the fact that the SHBT program was a success, and a clear asset to HST.

So, as of July 1, 1996, at the age of 67, I stepped down as the Director of EPL, but continued to be involved in its activities as a member of the MEEI Board of Trustees. I made a personal commitment to not interfere with policies introduced by new leaders of EPL but would be available to consult on science or career advice for faculty and students. Thus ended the early history of EPL, with later doings firmly in the hands of the next generation.