S. Murray Sherman

Born:

Pittsburgh, Pennsylvania
January 4, 1944

Education:

California Institute of Technology, BS, Biology (1965)
University of Pennsylvania, PhD Anatomy (1969)

Appointments:

NRSA Postdoctoral Fellow, Department of Physiology, Australian National University (1970–1972)
Assistant Professor of Physiology, University of Virginia (1972–1975)
Associate Professor of Physiology, University of Virginia (1975–1978)
Professor of Physiology, University of Virginia (1978–1979)
Professor of Neurobiology and of Anatomy, Stony Brook University (1979–1990)
Newton-Abraham Visiting Professor, University of Oxford (1985–1986)
Dr. Lee Visiting Research Fellow of Christ Church College, University of Oxford (2000–2001)
Leading Professor of Neurobiology and of Anatomy, Stony Brook University (1990–2004)
Maurice Goldblatt Professor and Chair of Neurobiology, Pharmacology, and Physiology, University of Chicago (2004–2006)
Maurice Goldblatt Professor and Chair of Neurobiology, University of Chicago (2006–present)
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Honors and Awards (Selected):

A.B. Sloan Fellow (1977–1980)
RCDA Recipient (1976–1980)
University of Oxford, MA, Honorary, (1985)
Guggenheim Fellow (2000–2001)
Editor-in-Chief, *Oxford Research Encyclopedia (ORE) of Neuroscience* (2015–present)

Murray Sherman has devoted his research career to the study of thalamic and thalamocortical circuitry. His efforts have led to elucidating the circuitry of the visual pathway from retina through thalamus to cortex. He and his long-term collaborator, Ray Guillery, are responsible for the introduction of the classification of glutamatergic pathways into driver and modulator categories necessitating a revision of previous ideas about circuit function. They also discovered transthalamic pathways in which direct connections between cortical areas often are paralleled by a cortico-thalamo-cortical route, the importance of which is increasingly appreciated by the neuroscience community. Finally, Murray Sherman is the founding chair of the Department of Neurobiology at the University of Chicago.

S. Murray Sherman

Preface

Although interest in the brain started well before recorded history, it could be argued that the explosive maturation of the field of neuroscience pretty much coincides with my career, from the late 1960s to the present. (This is a nice example of how a correlation does not necessarily indicate cause and effect.) When I started, "neuroscience" was not a phrase in common use. Instead, we referred to a plethora of terms that reflected the lack of unity of the field at the time: "neuroanatomy," "neurophysiology," "psychobiology," "biopsychology," and others. There were no neuroscience or neurobiology departments. Instead, brain research was largely carried out in medical schools, in anatomy or physiology departments, or in undergraduate psychology departments. As a result, the operative subgroups were pretty much separated from one another. Now, of course, research universities commonly have departments totally dedicated to neuroscience, although some are called "neurobiology" and others, "neuroscience." Furthermore, many universities now have institutes or centers that provide umbrella support for neuroscience spanning conventional departments. Over this period of increasing interest in neuroscience the Society for Neuroscience (SfN) grew from a few hundred members in 1969 to 35,000–40,000 today. The point is that the field has matured so that neuroscience is now regarded as among the most important academic subjects, in part perhaps because the growth of the field has incorporated many nonbiological disciplines, such as mathematics, physics, chemistry, engineering, computer science, and economics. This is my perspective of the larger environment in which my career developed.

I am impressed with the sophisticated understanding shown by today's students with regard to career options available to them. In contrast, as I recall, my view and that of my friends at early stages of our careers was poorly informed and generally feckless. Speaking for myself, when I entered graduate school, I had little or no understanding of the National Institutes of Health (NIH) or the National Science Foundation (NSF) or any idea of what being an academic scientist entailed beyond romantic ideas of "eureka" moments more informed by Hollywood than reality. Today's students are extremely well informed and have a pretty realistic understanding of the challenges that an academic scientific career holds for them. However, I worry that they extrapolate from their enhanced understanding the sense that they have reasonable control over their career paths. If my story has any value for such students, I hope it is the understanding that

several critical outcomes in their careers will be determined by factors not under their control but rather by chance and, therefore, that success will also require a large portion of plain good luck.

In the text that follows, I try to emphasize the various factors that molded my career, and perhaps most important among them is serendipity. This starts with having an early family environment that encouraged education and a wife who strongly supported my career choices; it continues with teachers and scientific supervisors who not only provided needed training and role models but also promoted my further career by helping with placement at the next stage; and it ends with having high-quality collaborators throughout my career, both in the form of my predoctoral and postdoctoral students as well as a long-time outside collaborator in Ray Guillery (more on Ray to come). I suppose the underlying message to follow is that luck will show itself at various stages in one's career, and one has to recognize and take advantage of such occurrences.

Personal History Notes

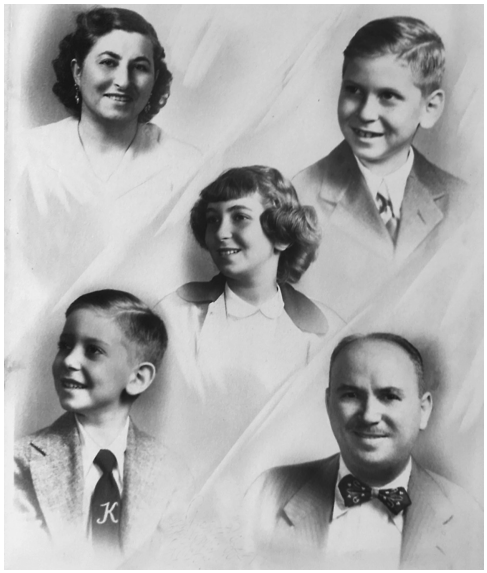
Early Upbringing and Career Choice (1944–1961)

My early upbringing was pretty unremarkable and, frankly, a bit boring, and so I'll keep this bit brief. On January 4, 1944, I was born in a Pittsburgh hospital to a fairly conventional Jewish family, but we lived at that time in Carnegie, a mill town just outside Pittsburgh. I have an older sister, Pepi, and a younger brother, Leon. Because of several anti-Semitic incidents in Carnegie (including a second-grade teacher who berated my cousin and me in front of the class for being Jewish, because Jews murdered Jesus), we moved to the Squirrel Hill district of Pittsburgh, a largely Jewish enclave, when I was eight years old.

My paternal grandfather emigrated from a small town in central Europe, arriving at Ellis Island in 1885 at the age of 25. His name then was Marcus Schermer, but somehow the last name was changed to Sherman, a common occurrence at Ellis Island. The name change might be related to the popularity then of General William Tecumseh Sherman; at least that's the family story, and I'm sticking to it. Marcus developed several small businesses, the most successful of which, a tire shop in Carnegie, he turned over to the partnership of my father, Julius, and his brother, Jacob. My mother, Ida, was born in Pinsk, Belarus, and came to America with her recently widowed father when she was one year old.

My parents, neither of whom advanced beyond high school, provided a stable environment and strongly encouraged education. In my father's case, opportunity for university education was there. He was valedictorian of his high school class, and he and his brother, Jacob, were all-state football players in high school. As a result, he was offered a full scholarship to play

football at Penn State. However, he and Jacob, as the oldest sons, were put to work helping their father in his business ventures. This happened partly because my grandfather needed help with his growing business and wanted to keep it in the family and also because university education was not then seen as so important to business careers as it is today. This also made it possible for the next two sons, Ben and Sam, to become a lawyer and doctor, respectively, which they did. This was the typical Jewish family plan: have at least two sons, with one becoming a doctor, and the other, a lawyer.



My family in 1951. I'm at the upper right.

Thus, in typical Jewish tradition, my parents had the same plan for their children: I, as the first son, was to become a doctor, and my younger brother, a lawyer. My sister is perhaps the brightest among us, but women then were supposed to settle down as wives and mothers, not pursue careers, and so she did as expected: she married young and had three girls, but her marriage has been happy and her daughters have all developed into successful, lovely women. In any event, and as a testament to my parents' encouragement, all three of us children graduated from university. My brother also followed the plan by graduating from law school, and he has enjoyed a successful law career. I did not follow the plan, as I ended up with a PhD instead of an MD. My mother never really accepted my career choice, and until the day she died, at which time I was a fairly successful senior scientist, she would typically greet me with the plea to go back to medical school to become a real doctor.

I always did well in school, from 1st through 12th grade (no kindergarten then in Carnegie). I had lots of friends and was active in sports to

offset my nerdy, scholastic side. My last fistfight was in third grade against Bernie Marcus; we had argued over who was better at drawing horses. Overall, my upbringing through high school was fairly ideal and short on nasty dramatic incidents.

My early decision to pursue a science career started with the intersection of two events. One was a superb and inspiring high school physics teacher, Mr. Norris, and the other was Sputnik. The former made science, and especially physics, seem like an ideal career choice, and the latter—the satellite launched in 1957 by the USSR, an event that shocked and worried Americans—led to a patriotic call for more scientists. So I decided that science generally and physics in particular would be my calling.

Caltech, Pasadena (1961–1965)

I researched which colleges offered the best physics training, and I chose Caltech. I frankly cannot remember why I chose Caltech, because Mr. Norris and other school advisors recommended the Massachusetts Institute of Technology (MIT) or an Ivy League school, but I do remember having my heart set on Caltech for whatever reason. Being able to attend Caltech meant convincing my parents of my choice. They had never heard of Caltech, which was more than 2,400 miles away in Pasadena, California, and thought nearer choices, like MIT or, better yet, Carnegie Tech in Pittsburgh (it became Carnegie Mellon University in 1967), would suffice. In the end, they relented, helped along no doubt by a generous scholarship offered by Caltech. I started there as a freshman in the fall of 1961.

Caltech was a special place for an aspiring young scientist, as I imagined myself to be. Very few students were accepted: there were about 150 or so in my freshman class. I suddenly found myself among incredibly brilliant peers. This was both inspiring and daunting—inspiring because the friends I made were so talented and served as wonderful early role models for me, and daunting because I was used to being the brightest student in my class, and now I was just average, at best. I noted that a number of my student acquaintances transferred after their freshman year to local, less elite universities, and the word was that they needed again to be thought of as tops in their class. I suppose this was a good experience for me, because if I couldn't handle being average intellectually in my group, I would find my situation even more depressing when I became a research scientist. We often overlook the fact that our scientific peers are an especially brilliant subset of human beings.

Being a Caltech undergraduate was my first experience away from home, and quite distant at that, so casual weekend visits were not in the cards. Southern California and the Los Angeles area took much getting used to, and this period coincided with the height of the new surfing culture. I also arrived knowing exactly zero people there. I remember my friends in high school choosing colleges based at least partially on having friends there. And so my

choice of Caltech would seem to be a recipe for homesickness and depression, but for whatever reason, I never thought about that, and it never bothered me. To the contrary, I rather enjoyed my new freedom, and I absolutely loved the fact that I made new friendships that were quite different from those I developed growing up in Squirrel Hill. Most of my friends through high school fit into a rather homogeneous group—mostly Jewish and rather conformist, although I thought highly of them and still do when I think back. Caltech students had only one thing in common—their brilliance—but otherwise I was exposed to new friends with backgrounds entirely novel to me, including the first foreign born, the first Asian, the first Mormon, and the first farm-raised. (But no African Americans and few Hispanics: Caltech was at that time pretty much white and Asian.) The students there also raised the culture of nerdiness to new heights, but whereas such types were rather shunned in my high school, here they were the norm, and I came to respect that.

A crisis arose early in my sophomore year. My father suddenly died of a massive heart attack. He had one heart attack a few years previously, but I had thought he was fully recovered from that and in reasonably good health, so this was quite a shock. It almost led to my dropping out of Caltech for two reasons. First, my state of mind was not hospitable to education, and I stopped going to classes for a period. My grades suffered. In the nick of time (or so I believe), I pulled myself together and managed to stay afloat. I once again attended classes and studied, and my grades rose back to normal, so I survived this part of the crisis.

The second reason was financial. My father had kept the family finances pretty much to himself, and when he died, we came to realize that the family's financial state was poor. I thought I would have to drop out of Caltech and get a job, but my mother would have none of that. How she coped, I'm not entirely certain, but she managed to support my continued stay at Caltech. This lasted for a few years, when financial fortune struck. She met an older widower at my cousin's wedding—he, the widower, was an uncle of the bride. He was also very rich. They married, and my mother's financial woes ended. I was grateful for that and for the fact that the marriage made my mother happy, but I did not care much for the man. He was Jewish (of course) and would later treat my wife rather badly because she is not. He died a few years after our wedding and left my mother comfortably off for the remainder of her life, so she could move to Florida and mingle among friends during her final years.

I graduated from Caltech with excellent grades despite my sophomore slump. While I was a student, all Caltech undergraduates were male, since women were not finally accepted as undergraduates until 1970. I believe the consensus at the time was that date-eligible young women with any sense avoided us like the plague. Finding suitable female companionship became an ongoing and generally fruitless activity. This was somewhat exacerbated by the proximity of Pasadena City College, from which the Rose Bowl Queen

was chosen each year for the annual New Year's Day Parade. Many beautiful young women enrolled there to be eligible for such royal status, but Caltech was clearly off limits to them. Finding such pulchritude nearby but off limits was frustrating to the extreme. Chasing hopelessly after female companionship led to an awful lot of wasted energy that would have been better spent studying physics.

One skill definitely lacking among Caltech undergraduates was athleticism. This, plus the small student body, enabled me to indulge in my love of sports. Thus, the first two years, I played varsity football, baseball, and basketball. Caltech was notoriously deficient in all three varsity sports, hardly ever winning and with losing streaks often measured in decades rather than games or even years. I remember the team winning a football game on a Saturday against a nonconference rival, the Bible College of Los Angeles. This was the first football win in a decade or more, and needless to say there was a tremendous celebration on campus that weekend. Our joy was short-lived, because, on the Monday, the president of the Bible College of Los Angeles announced that his institution was forthwith giving up its football program.

Three varsity sports took far too much time from studies, so after my sophomore year, I limited varsity sports to baseball. I remember the choice as being partly because it was the least dependent of the sports on others' skills: football and basketball rely more on teammates for success, and given the athletic quality of me and my teammates, winning even a single game in these sports was beyond hope. I thought baseball, given that I was a pitcher and thus more in control of the outcome, offered more chance of winning a game. In any event, we lost every baseball game anyway, which also says something about my skills as a pitcher. Such was sporting life at Caltech.

There is, however, one athletic record held by Caltech in football that seems unlikely to be broken. Some of our home games were played in the Rose Bowl, a cavernous football arena in Pasadena. Every Caltech game held there was played before more than 90,000 empty seats. I believe that no other college football program can boast such improbable attendance figures.

My senior year, I moved off campus with two other Caltech seniors as roommates, whom I have kept in touch with as friends ever since: Michael Rosbash, currently at Brandeis University, was trained as a molecular biologist and has made seminal contributions to neuroscience, leading to his receiving the Nobel Prize in 2017; and Arthur Niell, trained as an astronomer and currently at the MIT Haystack Observatory. Arthur's contribution to neuroscience was fathering Cris Niell, a rising star in the field of neuroscience.

Caltech has had an interesting association with the University of Chicago along several dimensions, especially with respect to neuroscience and me. My start in neuroscience as an undergraduate was working in the laboratory of Roger Sperry, who moved to Caltech from a faculty position at the University of Chicago (more on that later). Similarly, the current president of Caltech, Tom Rosenbaum, was provost at the University of Chicago

and as such played a key role in supporting the development of neuroscience when I arrived there. Finally, a surprising number of my faculty colleagues in neuroscience at the University of Chicago have Caltech ties: John Maunsell and Ruth Anne Eatock, both in my department, were graduate students at Caltech; and Dan Margoliash and Nicho Hatsopoulos, of the Department of Organismic Biology and Anatomy, also trained there, Dan as an undergraduate and graduate student, and Nicho as a postdoctoral fellow.

University of Pennsylvania, Philadelphia (1965–1969)

I started graduate school at Penn in 1965, working with Jim Sprague. A boyhood friend, Henry Berger, was a first year medical student at Penn that same year, and so we roomed together. Henry and I remained close friends until his tragic death from melanoma in 2011. That first year, there was a housing shortage for new students at Penn, and so the university purchased a decrepit motel, the University Inn, just off the medical campus, and with minimal renovations, turned it into a dormitory for first-year medical, dental, and veterinary students. I was accepted as Henry's roommate. This was an interesting experience from at least two perspectives.

First, the sociology of these entering students was fascinating to observe. There was a distinct pecking order, with medical students carrying off an air of superiority over dental students. Veterinary students were hard for the others to characterize, but when it was revealed that they had better overall scores and grades than medical students, and several turned down medical school places to become veterinarians, they rose to the top, but they didn't seem to care, which baffled the dental and medical students. As for me, being the only PhD student there, I was treated as a sort of exotic pet, and I rather enjoyed the whole experience.

The second interesting feature of life there was coming to realize what the University Inn was before being sold to Penn. Philadelphia is the site of a large naval base. On our very first weekend there, a group of sailors showed up in the evening, with their ladies of the night, expecting to rent a room by the hour as they had in the past. When they discovered that the motel had transitioned to a dorm, they attempted bribery to secure a room anyway. Henry and I were tempted but declined. This went on for several more weekends until the word finally spread throughout the U.S. Navy that University Inn was no longer a trysting site.

In 1968, while still a graduate student in Philadelphia, I met my future wife, Marjorie. We married in 1969. I cannot overstate the importance of Marjorie to my career. She has been unfailingly supportive, bore the brunt of raising our children as a wonderful mother, and later worked in my laboratory as a manager and administrative assistant. She has been a great help in editing manuscripts, although in one case, we failed her. She proofread the first book I wrote with Ray Guillery (Sherman and Guillery 2001) and did so flawlessly.

The one section she did not proofread was the Preface (because we submitted it rather late to the publisher). We included acknowledgments here and wrote: "Majorie Sherman helped with the proofreading."

There was one unfortunate aspect to my relationship with Marjorie. My family, extending to aunts, uncles, and cousins, were all serious about their Jewishness. Marjorie was raised as a sort of nonreligious Christian, and neither of us has been religious as adults. To much of my family, it was considered unacceptable for me to marry a *shiksa*, which is a rather disparaging term for a non-Jewish female. My sister and brother immediately accepted Marjorie as my future wife, and my mother did, grudgingly at first but, after getting to know Marjorie, without reservation. As I wrote earlier, my mother's second husband never accepted Marjorie and refused to attend our wedding. Even more disturbing, when we announced our engagement, I received a telegram from my uncles telling me that, because I was marrying a non-Jew, they were sitting *shiva* for me. Sitting *shiva* is a Jewish rite that effectively means that I was dead to them. Even though growing up I was fairly close to my uncles, I never spoke to them again after this.

I received my PhD from Penn at the end of 1969.

Australian National University, Canberra (1970–1972)

For my postdoctoral training, I signed up to work with Peter Bishop in Australia, starting at the beginning of 1970. An early part of my marriage with Marjorie was defined by what we saw as a great experience involving my postdoctoral training. Living overseas for two years added to the adventure. Furthermore, we purchased around-the-world air tickets that were good for going to and returning from Australia and allowed us at no added expense to make many stops along the way as long as each leg had an eastward vector.

Marjorie and me in Canberra.

We sold all of our belongings (which actually didn't amount to much) that didn't fit into our suitcases and set off on our great adventure. Marjorie had found an amazing travel agent through her aunt, who was a seasoned world traveler, and the agent provided us with a fantastic itinerary that we could afford (barely). Going to Australia, we visited Turkey, Greece, Uganda, Kenya, Tanzania, Thailand, and Hong Kong; returning, we stopped at Fiji and Mexico. At each place we were provided with a private guide, and in each case, the guide was competent and most informative.

The best part of the trip was the African leg that was entirely safari. We had great luck with animal sightings. However, we did have one scary episode. While we were in Uganda, there was considerable political unrest, and it was only a few months later that Idi Amin overthrew the elected government of Milton Obote. While driving through the outback in Uganda, there was apparently an attempted coup, a rather common event then, and we were stopped at a roadblock looking for rebels. The roadblock was manned by very young soldiers—teenagers at best—who carried impressive-looking assault rifles and seemed quite nervous and trigger happy. As they pawed through our luggage, they found my photographic tripod and apparently thought it was part of a machine gun. There was a lot waving of arms of and shouting in some Bantu dialect until our native driver managed to explain to them what the tripod in fact was used for. I haven't traveled with a tripod since.

The only other downside to our extended safari is that I used to love visiting zoos, but after Africa, I find them uninteresting and depressing.

When we reached Canberra at the end of our travels east, we were to be met at the airport by Peter Bishop. We arrived with about $20 between us, having exhausted our fortune on our journey, and the airport was empty. No Bishop, and we had no phone numbers of anyone to call. There was a hint of panic setting in, but Bishop did arrive a bit late, and we heaved a collective sigh of relief. I believe that point was the nadir of our financial status—it's been uphill ever since.

We were given housing in a suburb of Canberra, called Garran, in the Woden Valley. Garran was a collection of newly built bungalows owned and operated by the Australian National University (ANU). For Marjorie and me, this was a rather luxurious upgrade from the seedy apartments we occupied in Philadelphia, seedy because our combined incomes didn't support better. The two-bedroom house we occupied in Garran was roomy, airy, and completely furnished down to knives and forks in the kitchen. Most of the residents we met in Garran were postdoctoral fellows in various areas at the ANU, and it was often referred to affectionately as the "Garran Ghetto." Our neighbors included Peter and Stephanie Hoffmann plus Jonathan and Margaret Stone; Peter, Jonathan, and I collaborated on research in Bishop's group (more later). The Hoffmanns, Stones, and Shermans became fast friends.

Finances limited our travel within Australia, but we did manage excursions throughout much of the states of New South Wales and Victoria, and we also went on a magical trip to Tasmania. Furthermore, getting to the outback from Canberra was easy, and we often explored the interesting landscapes and animal life there. We were fortunate to have a Garran neighbor, John Baldwin, a zoologist at the ANU and an expert on the outback, to serve as our guide on numerous expeditions. Whereas Canberra remains the only capital city in Australia not sited directly on the coast, an interesting two-hour drive over a small mountain range brought us to Bateman's Bay, a beautiful, nearly deserted, pristine beach—deserted in terms of humans but not kangaroos and wallabies.

I found that the language barrier there was surmountable and managed it reasonably well. I even learned the jargon associated with cricket. Often, however, I found English usage there somewhat puzzling. For instance, my first experiments there were intended to extend my graduate work, and this involved very delicate brain surgery on cats (e.g., splitting the optic chiasm). To support this, my mentor, Peter Bishop, told me he had arranged time in surgery for me, but also said that he would assign a trained "theater sister" to assist me. I couldn't understand why a nun with acting experience would be much help. On a similar note, we were bemused by the fact that *Sesame Street* was a newly popular program in Australia, and there was much complaint among parents that their children were learning and using foreign terms: "cookie" instead of "biscuit," "wastebasket" instead of "dustbin," "sweater" instead of "jumper," "gas" instead of "petrol," "flashlight" instead of "torch," and so on. But after a while, I became fairly fluent in the language.

As my postdoctoral period came to an end in early 1972, we needed to return to America and that meant that I must seek an academic position there. My preference, of course, would be a tenure-track faculty position at a university that would support my presumptive research career. I became acutely aware that I was greatly disadvantaged because of my geographic location: no American university would pay to bring me from Australia for an interview.

University of Virginia, Charlottesville (1972–1979)

Fortunately, serendipity intervened. Jim Sprague generously provided a postdoctoral spot at Penn for me to return to America from which I could find my first faculty position, which also owed much to his help (see later). Thus, in July 1972, I started as an assistant professor of physiology at the University of Virginia. Marjorie and I set up home in Charlottesville, where our two children were born: Erika in 1975, and Benjamin in 1978. Both received university degrees and have excellent, stable jobs. Erika works in computers for an advertising firm and lives in Detroit, but she has a second increasingly successful career as a techno musician, a calling that frequently takes her to

many American cities as well as overseas to perform.[1] Ben works for Epic in computer support, and lives in Madison, Wisconsin.

Erika was born with a very clear case of esotropia (her eyes were crossed). I thought the best course of action would be to seek advice from the chair of ophthalmology at the University of Virginia Medical School, but I was wrong. The advice was just to wait, and if by the time she was six the problem remained, surgery could then be done to correct it. Fortunately for Erika, much of my research involved visual development inspired by work of David Hubel and Torsten Wiesel that defined the concept of an early critical period for visual development. I thus knew that to wait for six years at the beginning of life would likely mean that Erika's vision in one eye would be dramatically and permanently impaired. Also fortunately, I had heard of Marshal Parks, a pediatric ophthalmologist in Washington, DC, who understood the concept of the critical period and thus championed early intervention for vision defects like esotropia. So, we took Erika to see him, and he performed corrective surgery to straighten her eyes when Erika was a little over six months old. I'll never forget how difficult and traumatic it was to then hand over our baby to the surgical team. Nonetheless, and despite the fact that three minor corrective surgeries were later needed, overall this proved successful: Erika now enjoys excellent vision in both eyes.

My discussions with Parks during this period of treatment for Erika were quite revealing. He told us that, as a pioneer in respecting the critical period, which challenged then conventional treatment of no intervention for the first few years, he rattled a lot of cages that resulted in much negative feedback for him. He eventually prevailed, and now it is common practice in pediatric ophthalmology to attempt corrections of abnormalities like strabismus or cataract as early as is safely practical. Nonetheless, this served as a useful example of a problem regarding the recognition by clinicians of relevant basic research findings.

Charlottesville was a good place for Marjorie and me to reestablish ourselves in America. Charlottesville and the University of Virginia campus are historical and picturesque, and the beautiful countryside nearby, particularly the Blue Ridge Mountains, are quite appealing. Living in a small town like Charlottesville was pretty easy and stress-free. However, we felt a bit like the place was haunted by the ghost of Thomas Jefferson, who had lived nearby in Monticello and established the University of Virginia. Charlottesville residents continue to idolize him. While we were there, it seemed that any important decision made by civic or university leaders was first vetted by imagining what Mr. Jefferson would have done.

Eventually, the lack of cultural diversity in Charlottesville wore on us. For instance, the one local Mexican restaurant served black-eyed peas instead

[1] See Interdimensional Transmissions, http://interdimensionaltransmissions.com/artists/erika, and Resident Advisor, https://www.residentadvisor.net/dj/erika.

of refried beans. The town and university had few people of color. During the school year, local movie theaters showed typical Hollywood fare, but in the summers, when much of the University community departed, this fare was largely replaced by hillbilly porn. Perhaps unfairly, we worried a bit about raising children in this environment. Given this, the opportunity to relocate to an area culturally in the domain of New York City seemed quite compelling. And so we moved to Long Island.

Stony Brook University, Long Island (1979–2004)

After seven years in Charlottesville, I took up a position at Stony Brook University. And so we moved in 1979 to the small village of Belle Terre, just outside Port Jefferson, which in turn is just east of Stony Brook, on the north shore of Long Island. We spent 25 years there. Our home was a few hundred yards from the beach, which was privately owned and maintained by Belle Terre strictly for its residents. We spent much time on the beach and exploring the bucolic east end of Long Island. Life there was very good.

We had expected when we moved to Long Island that we would spend much time in Manhattan. But this turned out to be an unrealized goal largely due to the combined ineffectiveness of the Long Island Railroad and Long Island Expressway. The former took nearly two hours, and an unreliable two hours at that, and the latter could take much more time; both are testaments to our national failure to maintain infrastructure. As a result, after the first few years, we more or less ignored Manhattan except for very special occasions.

The area of Long Island we lived in was a bit unusual politically and culturally. It has a long history, being settled mostly by the English in the 17th century. There was strong Tory (i.e., British) support during the Revolutionary War, and even when we lived there, the local population seemed quite conservative politically. Culturally, the area was predominantly white, with very few people of color. Into this mix was thrust Stony Brook University, which occupied its present campus in 1962. This brought to the area the expected liberal and diverse culture, and to us it seemed that the university was never completely welcomed by the residents. This created a "town–gown" divide. One result was that amenities usually associated with university domains, such as culturally diverse theater, music, and restaurants, were slow to develop.

Our children basically grew up on Long Island and left home to establish their current career paths, starting with university. With this, we experienced an "empty nest" lifestyle. This made it easier for us to leave Long Island when I took up my present position at the University of Chicago. Of course, the main attraction for me was a leadership position in developing neuroscience at a great institution.

University of Chicago (2004–present)

The move to Chicago marked a dramatic change in life style for Marjorie and me. This was our first experience in big city living since our earlier experience in Philadelphia: Canberra and Charlottesville are small towns and Belle Terre is barely a village. We moved to Chicago without much knowledge of the city itself: neither of us had spent any appreciable amount of time there, not counting endless periods of waiting at O'Hare airport for flight delays. So it was a delightful surprise to discover the city of Chicago and come to realize that we love living there. It seems to us like a much cleaner and friendlier version of Manhattan, with wonderful architecture plus excellent music, theater, and restaurants. We also love the fact that the frontage along Lake Michigan from south of Hyde Park north almost to Evanston has been kept pretty free of private development and, as a result, is one long park. The lakefront is a source of beautiful recreation much admired by the people of Chicago. We quickly adapted to city living.

We settled in the Hyde Park section of the city, where the University of Chicago is located and which is about six miles south of the city center, right along Lake Michigan. Houses are hard to find in Hyde Park, and so we spent the first two years there living in a university-owned apartment, all the while looking for a house suitable for us. After two years, we did so and moved into our present abode. I love the fact that this provides me with a 12-minute walk to my office. Our move to Chicago also places us closer to our children: Erika lives in Detroit and Ben lives in Madison, Wisconsin. We get to see them much more often than we did while we were living on Long Island.

Hyde Park is ethnically and racially quite diverse. It is dominated by the university, and roughly two-thirds of the faculty live in Hyde Park. It is thus a sort of academic ghetto. But Hyde Park also includes a large

The Sherman family in Chicago. From left: Erika, Benjamin, Marjorie, and me.

segment of non-university people. What is odd (to me) is that a large and vocal segment of Hyde Park residents resents the university and sees it as an undesirable element in the area. This seems partly to stem from the fact that the university is a major landlord, owning many of the residences and properties rented out to various businesses, and so the university is a vehicle for change, which is not acceptable to many. I suppose these sorts of town–gown conflicts are inevitable.

Oxford University (1985–1986, 2000–2001, 2010)

I took three sabbaticals, all at Oxford University in England. The first two (1985–1986 and 2000–2001) were for a little more than 12 months, and the last (2010) was for the summer. For the first one, Marjorie, Erika, and Ben all came with me, but for the last two, our children were out of the house, and so it was just Marjorie and I.

The city of Oxford and its university present a spectacular scene, with its numerous colleges housed in buildings of architectural and historical splendor, many of the buildings being in constant use for centuries. Oxford University is sort of like Disneyland for academics.

There is no American equivalent to Oxford University, so it takes some explaining. The university is a rather loose confederation of its colleges. There are 30–40 Oxford Colleges, unclear to me exactly how many, because the exact number seems to depend on how various Oxford establishments are classified. The college is the academic heart of the university, and undergraduate hopefuls apply to a college, not the university, for a place. The colleges are quite variable in size, stature, and history. For example, Lincoln College is a fairly small college, currently with 35 fellows (the equivalent of faculty, although the actual term varies among colleges), whereas Christ Church College currently has 53 fellows (although at Christ Church, these are rather confusingly known as "students"). The oldest colleges were formed in the 13th century, and the newest, in the 20th. Much of the fortune at Oxford University is concentrated in the colleges, and the older ones are generally the wealthier.

Each college acts as a nearly independent academic unit. It provides room and board for most of its students and fellows. The meals, especially dinners, can be quite splendid in some of the wealthier colleges: Fellows dine berobed at high table in medieval splendor. Also, these same colleges have extensive wine cellars where fellows are offered premium wine, brandy, and port, at huge discounts. It is said that as impressive as the stately and historic architecture of the colleges is above ground, the cellars are even more impressive. Most teaching is done in the college by fellows leading "tutorials" with students, typically just three to four students per fellow at each tutorial, and this is supplemented by classes provided outside of the college by traditional academic departments. The tutorial system means

that each college must have a range of fellows able to cover the range of requisite topics. Thus, Oxford Colleges are built for breadth of subjects rather than depth.

If, during a prolonged stay, one is lucky enough to obtain a visiting fellowship at one of these colleges, as I did, then one benefits from the same privileges, above and below ground, as enjoyed by the permanent fellows.

First Sabbatical (1985–1986): A wonderful family experience for us involved my first sabbatical in Oxford with my long-term collaborator, Ray Guillery, from August 1985 to September 1986. I had a special and rather extravagant fellowship—the Newton-Abraham Visiting Professorship—organized by Ray. He was chair of Human Anatomy and in a position to deliver such a splendid appointment for me. The fellowship was generously supported by a trust based on the proceeds from royalties associated with the discovery of cephalosporin at Oxford University by Edward Abraham and Guy Newton. They were working in the group headed by Howard Florey, who, along with Alexander Fleming working separately in London, was credited with the discovery and clinical development of penicillin. The fellowship included a beautifully furnished modern house on the edge of University Parks, an ideal Oxford location close to the science area, as well as a visiting fellowship in Lincoln College. Having been founded in 1427, Lincoln College is rolling in wealth, and at the time of my sabbatical, was the richest college per fellow.

The appointment also led to my receipt of an honorary MA from Oxford University at the beginning of my fellowship. This involved a brief ceremony held entirely in Latin during which I had to provide a short speech prepared for me, also in Latin. I had no idea what was said to me or what I said, but no one present seemed shocked, which means either that their Latin was no better than mine or that I did okay. It all reminded me of my Bar Mitzvah.

Being a fellow at Lincoln College was a real treat for me. Its wealth was a significant factor in my sabbatical, because its fellows were treated generously and had access to the college's dining hall and wine cellar. Regarding the former, Lincoln had one of the best chefs in all of England, and so I very often had lunch, and occasionally dinner, there (family obligations limited these feasts, and except for rarely held special dinners, spouses were not welcome). Lunches were attended by many or most of the other fellows, and because of the breadth of disciplines covered by the fellows noted above, this meant lunch interactions involved learning something, often rather eclectic, about a wide range of academic disciplines. One day I might have lunch sitting next to an Egyptologist, the next day, a nuclear physicist, and the next, an economist. For me this was very different from my experience at American institutions in which we tend to interact nearly exclusively with colleagues working in fields close to our own.

My first sabbatical expanded my horizons in addition to the scientific ones I gained from association with Ray and other top academics there.

My devotion to the Lincoln College wine cellar provided me with a real education of the best French wines and an appreciation of good port. I learned how to eat a banana with a knife and fork, which I understand is very proper.[2] Indeed, this is how Queen Elizabeth II eats bananas. Also, I learned (sort of) to punt, and by this I don't mean kicking an American football but rather using a pole to propel a boat down a stream.

For me, the benefits of the sabbatical, in addition to my enological schooling, involved my association with Ray: The time spent together took our collaboration to a higher, more intense level. But there were others at Oxford that also contributed to my academic development, particularly Tom Powell and Kevan Martin. Ray gave me an office in his department that was next to that of Tom Powell, a celebrated neuroanatomist working on the mammalian visual system. I was cautioned about Tom before my arrival. For instance, Jim Sprague, an old friend and colleague of Tom, warned me that he was a major curmudgeon who often could be quite harsh with those he took a dislike to. For whatever reason, in my case, Tom was nothing but pleasant and supportive; I had many interesting discussions with him about the visual system. However, I did see the other side of Tom, when Irving Diamond arrived for a several-month stay in Oxford the spring and summer of 1986. Irving shared my office at the time. Tom, again for whatever reason, seemed to dislike Irving—there was obvious history there of which I remain ignorant—and Tom was constantly and openly critical and dismissive of Irving.

Irving was one of the Old Boys, along with Jim Sprague, who helped me secure my first faculty position, and he remained a supporter. As anyone who knew him could attest, Irving was a quite a character and oversized personality; he was also a dapper dresser. During his stay at Oxford, he seemed to regard my personal appearance in terms of dress with patient disdain. After a few days, he insisted on taking me on a stroll through the main shopping area of Oxford around the High Street, whereupon he introduced me to his tailor, shirt maker, and bootmaker (i.e., English for shoemaker) with the urging that I avail of their services. This was too rich for me, so I resisted, but in the end, I relented enough to buy a pair of shoes from his bootmaker. Maybe Irving had a point: I still wear those shoes today, more than 30 years later.

The other important personal relationship I further developed in Oxford was with Kevan Martin. I had a productive interaction with Kevan soon after our move to Stony Brook: he came to work with us (mainly Mike Friedlander) to learn the technique of intracellular recording and staining individual neurons in vivo. We hit it off, and I was looking forward to interacting with him in Oxford, where he was working with David Whitteridge as a research fellow. We spent much time discussing issues of circuitry of the mammalian visual system. I particularly enjoyed sitting in on his recording

[2] See Etiquette School, "Banana, Plantain Etiquette," https://www.etiquettescholar.com/dining_etiquette/table_manners/dinner_etiquette/fruits/bananas.html.

sessions of visual cortex, where Whitteridge often stopped by for lengthy periods, regaling us with wonderful stories of his earlier life spent in India. But Kevan also became a close family friend, spending much time with Marjorie, Erika, and Ben, as well as with me, and he provided much useful insight into British culture.

For my family, and especially my children, the experience of living in another country with a different perspective on life was priceless. We traveled all over Britain, and we became enthusiastic Anglophiles. We particularly enjoyed the cathedrals and castles we wandered through. This included York Minster, which had a devastating fire in 1984 that pretty much destroyed its south transept and roof. This gave our daughter, Erika, an opportunity to demonstrate her artistic ability. Blue Peter, a very popular children's program on BBC television, announced a contest for their young viewers for the best designs of bosses to be used in the reconstruction of the damaged vaulted ceiling of York Minster. (Architecturally, bosses are ceiling knobs common to cathedrals with rib vaulted ceilings and are found at the intersections of the ribs; they are often intricately carved and colored.) The six best designs would be used. Erika entered a wonderful design that made runner-up, which was quite an achievement and made us proud.

My son, Ben, who was seven at the time, picked up a delightfully genuine Oxford accent. Soon after we returned home to Long Island and he began third grade, he brought home a note from his teacher telling us that he had a serious speech impediment and needed to see a speech therapist as soon as possible. (On Long Island, the word "dog" is pronounced "dwohog," and so you can imagine how strange an Oxford accent would appear to a local.) We could not convince the teacher that this was a case of accent and not impediment, so Ben was examined by the therapist who duly reported that he talked like an Englishman, which is not usually considered to be an impediment. Unfortunately, Ben soon lost his posh accent, but this whole experience may have inoculated him against developing a Long Island accent.

One hiccup was culinary: There were no Cheerios or grape jelly to be found in England for Ben and Erika, and these were major food groups they relied on. They were unable to breakfast suitably and had no proper accompaniment for their peanut butter. A partial solution involved several trips I had to take back to the United States. I thus traveled with our largest suitcase, empty, and returned to England with it filled with Cheerios and grape jelly. I worried that a U.S. customs agent might spot check my bags on entry and become very suspicious at the large empty suitcase, but fortunately that did not happen. However, on one of my return trips, a British customs officer asked to see the contents of my luggage and was positively stunned at the sight of the boxes of Cheerios and jars of grape jelly. I thought I'd be put up on smuggling charges. Fortunately, the agent accepted my explanation with understanding and humor (or humour?).

A final factor helped in acclimatizing us to Oxford. Tony Movshon and his family (wife plus young son and daughter, just like us) also spent the year on sabbatical at Oxford. The Movshons were housed just around the corner from us. Our families were already on very friendly terms before the sabbatical, and our close association with them during the year was just one more benefit added to the experience.

There were two dark clouds to the year for us. One was mad cow disease, which was discovered in England in 1986. We had eaten some British beef before the announcement, and that was a cause for concern. The symptoms may not show up for decades, which means that we and our children can never be completely sure that we don't harbor the infection. In any event, we do not actually spend time worrying about it. However, because we lived in England during this period, we are banned from giving blood. Perhaps the worst part of this for us was having to refrain from beef for the remainder of our stay there. The other concern was the Chernobyl accident, which occurred in April 1986. The fear was that an unfavorable wind would deposit a lethal, radioactive cloud over England. This, fortunately, did not occur, and the concern dissipated after a few weeks.

Second Sabbatical (2000–2001): For this sabbatical, it was just Marjorie and I. My stay there was supported again by a visiting fellowship from a prestigious college: I was the Dr. Lee Visiting Research Fellow of Christ Church College from August 2000 to September 2001. (Matthew Lee was an early 18th-century physician who was a member of Christ Church College and endowed the fellowship.) Christ Church College is similar to Lincoln College in terms of age, wealth, and the privileges it provided for its fellows. One difference is size, because whereas Lincoln College is among Oxford's smallest, Christ Church is among its largest. One of the privileges the fellowship afforded was a furnished apartment across the street from the College in a prime location within the city.

Ray Guillery was at this time a visiting professor at the University of Wisconsin, so although we continued our collaboration during this year, it was at a distance. My sabbatical instead was spent with Ian Thomson, a visual neurophysiologist then in the Department of Physiology at Oxford. At the time, Ian worked on ferrets, doing single-cell receptive field analysis of neurons in the lateral geniculate nucleus and primary visual cortex. I sat in on many of these experiments, but mostly served as a passive observer. Nonetheless, I gained much from this experience. I learned new ways to study visual receptive fields, and after my exposure to the ferret as an animal model for my future studies (I was considering a switch to ferret or mouse), I realized that, for my interests, I should look elsewhere. Perhaps more important, my scientific interactions with Ian, his students, and others at Oxford once again proved critical to the development of my theoretical framework underlying my research program.

Marjorie and I once again thoroughly relished our time in England. In addition to Oxford itself, we enjoyed the countryside, especially the nearby Cotswolds and beyond, and we particularly enjoyed long walks there. However, the year of our stay, England suffered from two major ecological disasters that limited our rambling. One was historic rainfalls that preceded our arrival and led to severe flooding. Many of the rights-of-way for walkers were vast lakes and thus impassable, and any long walk meant the likelihood of a certain amount of wading. The other problem was foot-and-mouth disease, a dreaded and deadly disease that particularly plagues cattle and sheep. Since many of the hiking trails in England involve rights-of-way through private land used for grazing of these beasts, and because one way of spreading the disease is through hikers carrying it from one field to another, many or most of the best hiking trails were closed for the year.

A special treat was our return home. We arranged through a special deal with the Cunard Cruise Line to return home on the *Queen Elizabeth II* in 2001. Traveling by ocean liner was a great luxury: lovely food, wonderful entertainment (mostly musical), and leisurely travel. We arrived on the piers of the Hudson River in Manhattan on September 4, 2001, exactly one week before 9/11.

Third Sabbatical (Summer 2010): My final sabbatical (so far) was briefer, covering the summer of 2010. Again, Marjorie accompanied me. I received support as a professorial fellow of St. John's College, which also afforded a furnished apartment in an excellent location within north Oxford. St. John's College was very much like Christ Church College in age, size, wealth, and generous treatment of its fellows. The fellowship was arranged by my host, Andrew Parker, a professor in the Department of Physiology and also a fellow of St. John's; Andrew performs single-cell analysis of neuronal responses in the monkey extrastriate visual cortex.

Oxford University and its colleges are largely shut down from normal functioning during the summer, and the lively academic environment is largely replaced by language programs in which students from the continent spend the summer in various colleges learning English. Thus one doesn't experience the intense academic milieu of Oxford in the summer months. However, this disappointment was more than offset by the benefits to my scientific thinking of once again interacting with Oxford neuroscientists. The fact that Ray Guillery had returned to Oxford as a professor emeritus meant that, for the first time in 25 years, we were physically reunited for an extended period allowing us to pursue our collaboration with greater intensity. But more than that, I was installed in the Department of Physiology by Andrew, and that meant daily quite productive discussions with him and others in the neuroscience community, including Kristine Krug, Andy King, Zoltan Molnar, Peter Somogyi, Paul Bolam, and Colin Akerman.

Serendipity

How I decided on a career in neuroscience, starting with my time as a graduate student, involved a lot of serendipity. It also involves serious name-dropping, for which I apologize in advance, but it is central to the story. Without considerable good fortune at several stages of my career, I would not have been invited to write this.

My decision ultimately to choose neuroscience for a career was taken during my Caltech years. Caltech students were required to take two full years of physics in their freshman and sophomore years. What made this especially memorable for us was the fact that Richard Feynman (Nobel Laureate and name drop #1) decided to teach us these two years as the sole lecturer. I believe ours was the only undergraduate class formally taught in a classroom environment by Feynman. He was a remarkable lecturer: creative, superb at explaining complex concepts, and especially entertaining. His lectures were one event that we almost never missed. Occasionally during class, he would interrupt his physics instruction with personal stories and sometimes career advice for us. Several times he suggested the following: that, while many of us came to Caltech to become physicists, the real scientific frontier, more challenging and interesting than physics, was study of the brain; we should consider going into brain research ("neuroscience" was a term for the future).

I would like to think that Feynman's suggestion had a decided effect on my career choice, and it may well have, but in truth, my memory of the impact of his proselytizing for brain research is somewhat questionable. In any case, after my first year, I needed a summer job, and because of its availability and possibly also because of Feynman's suggestion, I took up a position in the laboratory of Roger Sperry (Nobel Laureate and name drop #2). I liked it and stayed on for the next three years, until my graduation.

My time in his laboratory was well spent. I worked with a senior research fellow of his, Evelyn Lee-Teng, and my collaboration with her led to a *PNAS* publication (Lee-Teng and Sherman 1966). Sperry was an imposing, imperious figure who did not interact with me very much. Thus, in spite of the productive time spent in his laboratory, even after two years I wasn't sure that he knew that I existed. Imagine my surprise (and anxiety) when, at the beginning of my senior year, he called me into his office. The conversation I remember quite clearly, almost word for word, although I cannot guarantee that what is written below is an exact transcription:

> *Sperry*: I've been watching you [I feared the worst at this point]. . . . You show promise. If you're interested in a career in brain research, I'd like to offer advice . . .
>
> *Me* [much relieved]: As a matter of fact, I am interested in brain research as a career, and I've started to look at grad schools.

Sperry: Excellent. Which schools are you considering?
Me: Right now, my first choice is the University of Chicago.
[At that time, the University of Chicago had one of the few brain research programs I was aware of.]
Sperry: If you go to Chicago, I'll never speak to you again!

His response dumbfounded me. Being naïve and rather passive, I asked what he would suggest instead. He told me that I would do well to go to Penn to work with Jim Sprague. I did. I never learned with any certainty what led to his astonishing response to Chicago (or, for that matter, why he recommended Sprague), but I later found out that, as a junior faculty member at the University of Chicago, he was denied tenure—thus the relocation to Caltech. Perhaps he retained bitterness over this and developed sustained animosity to the University of Chicago. Of course, the irony here is that I am now at the University of Chicago.

Another case of serendipity involved my choice of postdoctoral training. I remained feckless in my plans for my career, except for the notion that I needed postdoctoral training. I flirted with various options, rather superficially, until one day Jim Sprague came to me and suggested that I go to Australia to work with Peter Bishop. I'm not sure where that recommendation came from, but I followed it. The serendipity came with respect to the Vietnam War, which was raging at the time. My 2S student deferment was about to expire, and to leave the country, I needed written permission from my draft board. They gave permission with the caution that I would likely be selected for possible drafting, meaning that I would have to report to the nearest military facility at my expense for a physical examination in preparation for being drafted. I decided to go anyway. After five or six months in Australia, I received a letter from my draft board requiring me to appear on the specified date at a military facility in Hawaii for my physical. The specified date had already passed by several months! This is because they sent the letter by surface mail, which took months to arrive. I was panicked, thinking that my no-show would result in extradition and prosecution, so I fired off a letter to my draft board (sent via air) explaining my absence and asking for another date. I never heard from them again. Rather than being drafted, I was able to resume my embryonic career. This was made possible only by the curious decisions of my draft board both to communicate either via surface mail or not at all and also to not pursue prosecution. It wasn't until my return to American soil via air ended with no U.S. marshal greeting me with a warrant that I felt completely safe.

These events at the beginning of my scientific career relate to two issues. First, for better or worse, my career path was largely dictated by unpredictable forces over which I had no control. The curious outburst against the University of Chicago by Sperry and his suggestion to opt instead for Penn and Sprague remains somewhat enigmatic, but I likely would have otherwise

started research training at the University of Chicago instead with unknown results for my career. The suggestion by Sprague to go to Australia for my postdoctoral training allowed me to continue my career, because if I had opted for the much more common and likely choice of an American laboratory for further training, my draft board's letter would have arrived in time, and I would have been taken from science into the military with a likely end to any further research training. Second, the reason I followed Sperry's and Sprague's advice was my rather passive, uninformed nature, which I find in stark contrast to today's students, who, to their credit, are much better informed and in charge of their careers. In my case, I regard myself as extremely lucky at the turn of events, but a lesson for all, I believe, is that successful academic research careers require luck: skill, intelligence, and hard work are necessary but insufficient ingredients.

Professional Positions

Graduate Training (1965–1969)

I entered the PhD program at Penn as a graduate student in the Department of Anatomy in the summer of 1965. My graduate training would likely be unrecognizable to current students. Science at that time (latter 1960s) was very different than now: It had a leisurely, laid-back style dominated by an "Old Boy" network; competition for grant money, high-impact publication space (impact factors were a future concept), and recognition was considerably less than today. Only one other neuroscience student, Dennis Stelzner, matriculated with me—Allan Basbaum and Peter Strick arrived a year or two later. So it was a very small program. Also, the neuroscience faculty component consisted only of very senior members: Jim Sprague, Bill Chambers, Peter Hand, Louis Flexner, John Liu, Adrian Morrison, and Elliot Stellar. Peter Sterling arrived a few years after I began as the only junior faculty presence in the group. Also, unlike a modern research department, anatomy at Penn had little in the way of recognized laboratories run by principal investigators. Instead, there were mostly communal spaces shared by all, such as a large histology facility, rooms for training animals, a microscope room, and rooms for basic electrophysiology. Thus, I didn't actually work in a laboratory cheek by jowl with other students and postdocs but rather worked mostly on my own in these spaces. In these regards, the department was very old fashioned.

One result of the makeup and character of the department was that it had few rules for graduate students, and I felt my requirements were mostly determined ad hoc. This suited me well. In this environment, I believe the most important lesson I learned as a graduate student came from observing my mentors, especially Jim Sprague, Elliot Stellar, Bill Chambers, and John Liu: They were wonderful role models for how

to behave as an academic and scientist. I would like to think that their examples served me well in this regard. What I did not get much from my graduate experience were examples of modern research laboratories and practices. In any event, I ended up with a thesis that was adequate (barely, in my opinion, so no more said about that) for my PhD in 1969.

However, my PhD in anatomy should come with an asterisk. When I arrived at Penn in 1965, the course for medical students in gross anatomy was under way. We could tell when the course was in session, because the air stank of formaldehyde and all the doorknobs were greasy. I decided immediately that I wanted to avoid taking the course. When the departmental chair, Louis Flexner, a small but authoritative figure, heard about my request, he called me into his office. He was rather annoyed at my attitude and asked for a good reason why I should avoid the course. My answer was that if I never took the course, I never would be expected to teach it. He burst out in laughter (a shocking relief to me) and said that was the best reason he ever heard, and he immediately gave me permission to skip the course. So I have a PhD in anatomy but don't know my whatever from my elbow.

Postdoctoral Training (1970–1972)

I experienced a different research environment when, at the beginning of 1970, I moved as a postdoctoral fellow on an NIH F32 fellowship to the Department of Physiology at the John Curtin School of Medical Research of the ANU in Canberra. Peter Bishop was chair of the department, and the department was entirely composed of laboratories working under his overall guidance on vision research. These were very active and productive laboratories run by creative and industrious colleagues: These included Bill Levick and Geoff Henry when I arrived, and Jonathan Stone soon afterward. Postdocs who were contemporary with me were Peter Hoffmann, Bogdan Dreher, Mark Dubin, and Brian Cleland; Ken Sanderson was the sole graduate student. For much of my two-year period there, Horace Barlow was present on sabbatical with Bill Levick, and he added much in the way of scholarly value. This was a dynamic group, and it was during this time, that I received real training in how to do research effectively.

It may be hard for students today to appreciate the quality of this laboratory group. Peter Bishop replaced John Eccles (a Nobel Laureate) as head of the department just before I arrived, so the department already had a superb reputation. At the time, the Bishop laboratory was considered one of the best in the world for vision research, its main competitor being that of Hubel and Wiesel. I find it somewhat sad and a bit bewildering that few students today know of Peter Bishop and his contributions.

My first research assignment was to help Ken Sanderson, then a graduate student, with his thesis experiments. This was my first opportunity to learn electrophysiology and single-cell recording, because Ken's

thesis was all about understanding receptive field properties of cells in the cat's lateral geniculate nucleus, the thalamic relay of retinal information to visual cortex. I had the good sense to understand that our roles were reversed: As a postdoctoral fellow, I was the trainee to Ken, even though he was a graduate student. In any event, Ken was an excellent trainer, and we published two papers together (Sanderson and Sherman 1971; Sherman and Sanderson 1972). After Ken, I moved on to work with Geoff Henry on receptive field properties of cat V1 cells. We investigated many receptive fields in great detail (Bishop and his colleagues in Australia were pioneers in the use of computers to analyze receptive field properties quantitatively), and I learned a lot from Geoff, even though no publications derived from this work. During my first year in Canberra, Jonathan Stone joined the group and was assigned his own laboratory. Soon after, Peter Hoffmann and I joined Jonathan and formed a productive team concentrating on properties of the parallel X and Y streams in the cat visual system, and I remained with Peter and Jonathan for the duration of my stay in Australia.

Much of the research I was involved in for my postdoctoral training represented my first experience at the grueling schedule required for the continuous recording from an animal kept alive in an anesthetized state for two or three days. This approach was one I followed for the next decade or so. Although that approach served me well as a mainstay to the beginning of my independent research career, I'm happy to say that experimental approaches in my laboratory evolved to be less physically grueling.

From a training point of view, two things about my postdoctoral environment strike me. First, experiments generally were not based on specific hypotheses to be tested. They were mostly investigations about how things worked without preexisting biases. Can we find any responses to the nondominant eye in geniculate cells? What are the detailed patterns of excitatory and inhibitory parts of V1 receptive fields? How similar are geniculate X and Y receptive fields to their retinal counterparts, and how do these change with eccentricity? Today, it seems that the powers that be (e.g., various granting agencies) dictate that good science must start with hypothesis testing. Second, and perhaps related to this unbiased approach to science, the Bishop style was based on a detailed quantitative study of parameters, with the idea that such detail could eventually uncover interesting principles. This dependence on quantification may be seen as the antithesis to the more qualitative approach that depends for success on great insight, ingenuity, and originality—not qualities present in all—plus good luck. The problem with this latter approach is that the requisite qualities for success cannot easily be learned or developed, whereas the approach involving observation with a strong quantitative focus can. In any case, I believe this is one important lesson I acquired from my postdoctoral experience.

There were several other striking features of my postdoctoral environment. One is that everyone in the department worked on similar projects,

all involving the cat visual system from the retina through the lateral geniculate nucleus to V1. Peter Bishop oversaw all of this somewhat loosely, allowing for considerable independence in approach, and in this capacity, he was also very supportive. This included three major laboratories: one headed by Geoff Henry, another by Bill Levick, and the third by Jonathan Stone. Working on similar problems provided benefits in the form of useful collaboration, but it also created some problems. Bill's group (including Brian Cleland and Mark Dubin) and Jonathan's (including Peter Hoffmann and me) worked on largely the same issues involving the parallel organization of X and Y pathways. Bill and Jonathan are strong personalities, and this turned into a sometimes-unpleasant competition that, frankly, detracted from the overall otherwise-excellent research environment. One example among many involved terminology: We referred to the cell types as "X" and "Y" (and, later, "W"), whereas Bill's group insisted on "sustained" and "transient" (and "sluggish"). As a testament to how unpleasant this became, several papers were later published representing these two points of terminological contention, papers notoriously lacking in collegiality (see Rowe and Stone 1977 versus Hughes 1979).

Perhaps the most unusually dramatic feature of the environment was the isolation of the Bishop laboratories from the rest of the world's scientific community. In those days, there was no internet, and journals arrived via surface mail, which took months to arrive in Australia (recall earlier about how this affected my military career, or rather, lack thereof). As a result, we operated in a vacuum with little or no idea of what the rest of the scientific world was up to. This is hard to imagine in today's internet-tempered research environment in which we are far too aware of what's going on in other laboratories, especially in those of our competitors.

One result of this is that the work in Bill's and Jonathan's groups on parallel processing was developed to a state of some maturity before being made public. Christina Enroth-Cugell and John Robson first described X and Y cells in the cat retina in 1966 (Enroth-Cugell and Robson 1966), but not much was made of this until various papers came out from the Canberra groups in the early 1970s (e.g., Cleland et al. 1971; Hoffmann and Stone 1971; Stone and Hoffmann 1971; Hoffmann et al. 1972; Sherman et al. 1972; Stone and Dreher 1973; Fukuda and Stone 1974). From my perspective, this new way of looking at the organization of the central visual pathways seemed to hit the field as a fully formed new concept from out of the blue. That novel, mature concepts could appear so suddenly seems quite unlikely today, when we know far too much about ongoing research issues at very early stages.

I saw the reaction to this firsthand at a memorable meeting held in Canberra in early 1972, just before I left to return to America. Many leaders in vision research attended, and a list of participants plus the proceedings were published in a 1972 issue of *Investigative Ophthalmology* (volume 11, no. 5).

I vividly recall the astonishment and responses of the visiting participants as one after another of us presented our research results on parallel processing. Because these accounts challenged views of visual processing current at the time, the responses were not always positive. This meeting effectively came at the end of my postdoctoral experience.

Overall, my postdoctoral period was very productive for me and made me a viable candidate for a faculty position when I returned to America. My name as author or coauthor appeared on nine research papers derived from my stay of two years in Canberra. I attribute much of this to the environment created by Peter Bishop.

University of Virginia (1972–1979)

When my postdoctoral period was nearing its end, I knew that I wanted to pursue an academic research career, which meant that my next move would be to secure a faculty position at a research-oriented university. I wanted to return to America. My prospects seemed up in the air, however, and my situation was further exacerbated by the fact that I was far from home. Fortunately, Jim Sprague anticipated the problem and continued to provide generous support for me. This was then demonstrated by his offer of a temporary position with him at Penn that would allow me ready access to appropriate positions in America. Marjorie and I arrived back in Philadelphia in March 1972.

Soon after, during the first week of April, I attended my earliest major meeting at which I could present my experimental results on research I had done in Canberra. This was at the annual meeting of the American Association of Anatomists held in Dallas, and I saw it as my first opportunity to present my credentials as a potential tenure-track faculty member. I was excited at the opportunity and viewed it as extremely important to my career development.

In those days, the SfN was still neonatal and not yet the dominant venue for neuroscience, and in any case, its meeting would not be held until fall. The anatomy meetings had, up to that time, actually been the main setting for neuroscience. There were still few if any neuroscience departments, and most of what we would consider today to be neuroscience was then housed in anatomy departments. Also, presentations at major meetings were different in those days. Posters were rare, and most information was passed on in the form of 15-minute talks. And talks were illustrated not by PowerPoint but rather by old-fashioned slides imaged by Kodak Carousel projectors. The norm was that, as the speaker before you started, you loaded your slides in the empty Carousel to be used for your talk.

As I started to load my slides, I was horrified to discover that they did not fit: my slides were mounted in Australia in thick binders designed for European style Zeiss projectors, and they were too fat for the Kodak equipment. I panicked.

There are two versions of what happened next, mine and that provided by Jon Kaas who had given the talk just before the current speaker. I'll try to give both. In my version, I realized that Jon had slides with the proper binders for Kodak projectors. I went over to him and explained my plight, and asked for his help. He jumped right in, and we proceeded to unbind both sets of slides and refitted mine in his binders just in time for my talk. In Jon's version, I went to him to ask to look at his slides. He thought that I was so enamored by his talk that I wanted to go over it again in more detail, but he was shocked as I began to tear his slides apart. In both versions, Jon did realize the problem and gallantly helped me to avoid disaster.

So, I had navigated my first test as a potential faculty candidate thanks to Jon. Soon after, I visited the University of Wisconsin to look at a faculty position there, but this failed effort will be described in more detail, because it represented an early attempt for Ray Guillery and me to get faculty positions at the same place. At that point, I did not expect to resume looking seriously for a faculty position until after the summer of 1972, the season then as now when most faculty hiring commenced. However, Jim Sprague then took matters largely into his own hands to set me up with possible positions immediately. Recall that the Old Boys network was still up and functioning at that time, and Jim was definitely one of the Old Boys. He was close friends with Irving Diamond of Duke University, another Old Boy and venerated neuroscientist, and the two of them explored their network to come up with a promising position for me at the University of Virginia. The two major neuroscience figures there who supported my hiring were John Jane and David Cohen. John was chair of neurosurgery and a close friend and associate of Irving Diamond, and I believe that was the link that mattered most. David was then a professor in the Department of Physiology, the department into which I was recruited as an assistant professor. David immediately became my mentor, and his tutelage was a catalyst to my successful transformation from a rather feckless and rootless wannabe to a respectable faculty member.

I quickly set up a productive laboratory, greatly assisted by my first graduate student, Jim Wilson, and I followed up research threads from my postdoctoral period. I was able to get NSF and NIH funding right away, and began publishing a steady stream of research papers. As a result, I was promoted rapidly, to tenured associate professor in 1975 and full professor in 1978.

The University of Virginia was a great place for me to begin my independent research career. My chair, Bob Berne, was a renowned cardiac physiologist and coauthor of a major medical textbook (Berne and Levy, *Physiology*). Although not a neuroscientist, he strongly supported neuroscience generally and me specifically. Although there were only two other neuroscientists in the department (David Cohen and John Hackett), other departments contributed to a small but collegial neuroscience group. This included John Jane, Sven Ebbeson, Ozzie Stewart, and Ed Rubel in neurosurgery as well as Steve Edwards and Lennart Heimer in anatomy.

Although the neuroscience community was collegial and of high quality, it was small and limited, and it became clear toward the end of my time there that the University of Virginia was not likely to invest more heavily in neuroscience to take it to the next level. Attempts to form a neuroscience department or even a neuroscience graduate program led nowhere. This particularly bothered David Cohen, whose attempts to develop the area at the University of Virginia were frustrated. In 1979, he was recruited by Stony Brook University to establish a new neurobiology department there. Harvey Karten, who was a close friend of David and later become one of mine as well, was then at Stony Brook and a key factor in the recruitment. David encouraged me to join him, and I was ready to make the move both because I was also frustrated by the limited future for neuroscience at the University of Virginia compared with the possibilities at Stony Brook and also because Marjorie and I were ready for a change of scenery. We made the move in the summer of 1979.

Stony Brook University (1979–2004)

Because of a misplaced sense that I needed to establish some independence from David, I chose to take a position at Stony Brook in the Anatomy Department rather than in David's. That was a nearly disastrous decision for me, because I immediately ran afoul of the chairman of that department, and after one year, I was again saved by a mentor: David offered me a position in his department, which I eagerly accepted.

Moving my laboratory to Stony Brook was greatly expedited by the fact that two of my senior postdoctoral fellows at the University of Virginia, Mike Friedlander and Larry Stanford, made the move with me. They did the bulk of the hard work in setting up the new laboratory and did so quite quickly and efficiently. Also, as noted earlier, after the first year at Stony Brook, we moved departments, from Anatomy to Neurobiology, involving occupation of a new space and meaning that the laboratory had once again to be broken down and reconstructed. As a result of the efforts and efficiency of Mike and Larry, we were able quite quickly to resume our experimental program.

This was an exciting time for me, for reasons apart from my own experimental program, because I was from the beginning able to work with David Cohen to build a new department from scratch, which obviously involved a lot of faculty recruiting. David did a great job in doing so, and thus I enjoyed being in a department filled with first-rate neuroscientists. In spite of the fact that the final result was a success, I did have differences of opinion with David concerning the faculty recruiting, including the strategy behind it. This made me realize that I was actually quite interested in the possibility of playing the role of leading the development of my own department if the right opportunity came along. Eventually, it did in Chicago, but I'm getting ahead of the story.

As the department grew, I benefited from interactions with virtually the entire faculty, but my closest colleagues during this period, besides David,

were Harvey Karten, who was already at Stony Brook when we arrived, and new recruits Craig Evinger, Paul Adams, and Lorne Mendell.

The department had a curious structure, as it was considered both part of the Medical School as a Basic Science Department and also part of the undergraduate College of Arts and Sciences, which was practicable, because the Medical School and undergraduate colleges were part of the same campus. This meant that David reported to two deans and that our teaching involved both medical students and undergraduates as well as graduate students. Despite the dual nature of the department, each faculty member had to be administratively in one or the other college (Medicine or Arts and Sciences). As I recall, only three of us (David, Harvey, and I) were appointed in the Medical School with 12-month contracts; the others were all Arts and Science faculty with 9-month appointments. This strange arrangement might seem to be a cause for concern and internal strife, but it became irrelevant. This was largely because David as chair, and Lorne as his successor, ignored the differences in appointment when it came to salary, teaching assignments, and so on.

Stony Brook University was an odd place academically. Overall, it was a second-rate institution, and I was often bemused at the relentless self-promotion by the leadership to claim first-rate status, but such shameless institutional self-promotion seems quite common in academia today. Despite the limited overall quality, there were some programs that were especially strong and decidedly first-rate. Among these were the sciences, especially physics, and mathematics. I would include the Basic Science Departments of the Medical School in this category. Unfortunately, the clinical departments, in my estimation at the time, were mediocre academically, and this severely limited our horizons as biomedical scientists. Also, despite the relatively rare situation of a medical center located at the undergraduate campus, few successful examples existed of programmatic cross-fertilization between entities. Thus, it felt like the potential to extend neuroscience more broadly across campus went unrealized, something that played a role in my later decision to relocate to the University of Chicago. Nonetheless, and much more important to me, I regarded the Department of Neurobiology at Stony Brook as outstanding, and so my immediate environment was nurturing and exciting.

An unusual aspect of my laboratory at Stony Brook was its makeup: it consisted almost entirely of postdoctoral fellows and technicians. I did have two graduate students during my time at Stony Brook, but they entered from other programs: Alev Günlük (now Erişir) from the psychology program and Iva Reichova, a transfer from Northwestern University. In my 25 years there, not a single student from our neurobiology PhD program entered my laboratory. This is particularly odd, because I had graduate students at the University of Virginia and currently do so at the University of Chicago. I would have been happy to have graduate students at Stony Brook, but none were interested in my laboratory. I never got a real explanation for this.

University of Chicago (2004–present)

I was basically very happy at Stony Brook, and by the time my stay passed the 20-year mark, I fully expected to remain there for the rest of my career. As noted earlier, however, I was on the lookout for the right opportunity elsewhere to build a first-rate program of neuroscience. I had several criteria to be met that set the bar for the right situation pretty high: The institution had to be top-notch; the leadership position (e.g., a department chair) had to be structured in a way that would not significantly impede my laboratory's research program; and there had to be widespread institutional support for further development of neuroscience.

I had looked at a few possibilities after 2000, but none met these criteria. And then the possibility of Chicago came up. This intrigued me, because the quality of the institution clearly met one of my criteria, but I was a bit concerned that as a neuroscience entity, the University of Chicago was not even on my radar screen at the time. However, during my first visit, I came to appreciate that there were in fact many superb neuroscientists there. The problem seemed to be that, because there was no neuroscience department or institute with control of hiring to follow any strategic plan for the development of the field, the neuroscience community was spread over a number of departments, both in the Medical School and undergraduate campus, and it was also spread over a number of subdisciplines. Thus, in my view, despite having real strength among individuals, the neuroscience community was broad but not deep, and because there were no critical masses representing any single research topic, the community was not well recognized.

The University of Chicago had made a strategic decision early in the millennium to significantly enhance neuroscience. The Medical School dean who hired me, Jim Madara, was a strong believer in neuroscience, and together we concocted a strategy to move forward. The ultimate plan had two parts: first, to create a new Basic Science Department of Neurobiology to establish an initial focus and strategic center for developing the field; and second, to form a Neuroscience Institute with real resources that could be the strategic center for developing neuroscience campus wide, by encouraging departments other than Neurobiology (e.g., Psychology, Statistics, and Organismal Biology and Anatomy) to recruit neuroscientists.

This was an ambitious plan that would require strong support from both faculty and the administration. Administration support was already in hand. To generate faculty support, which is a sine qua non at the University of Chicago for accomplishing anything as ambitious as we had in mind for the development of neuroscience, Madara formed a committee cochaired by Dan Margoliash and me to come up with a strategic plan. In the event, this meant agreeing to the plan Madara had already formulated. Dan's effort here was indispensable, and we were able to get widespread faculty support for this plan with considerable enthusiasm.

Thus, in my second year at Chicago, the Department of Neurobiology was created, which is no small feat and required lengthy hearings and approval by a very conservative faculty senate. We immediately and quite successfully started recruiting faculty. For the next step, we needed to establish the Neuroscience Institute, and things were progressing nicely regarding necessary funding for it when the financial crisis of 2008 hit. This put the establishment of the institute on the backburner, which at the time I viewed as only a delay. But then another crisis hit: Madara was replaced as dean by Ken Polonsky. Not knowing the new dean, I immediately worried that he would lack the passion for neuroscience shown by his predecessor and allow it to languish. In fact, Polonsky has been even more of an enthusiastic sponsor of neuroscience than Madara and supported the continuing development of neuroscience quite generously. We were back on track.

The next set of tasks involved securing the funding for the institute, which was done in due course, and then recruiting a director. The latter took considerable time and effort, but in the end, we succeeded in luring John Maunsell to the position. He arrived in 2015 and immediately succeeded in partnering with various departments to recruit top-notch neuroscientists. As I write this, things are definitely on the ascent for neuroscience at the University of Chicago.

Also, from the perspective of my own research program, the move to Chicago has been a boon. Whereas, I very much liked my time at Stony Brook and thought highly of my colleagues there, there has been an added benefit of my move to Chicago. That is, at Stony Brook, there was no research focus that was close to mine, so my efforts were pretty much isolated. At Chicago, we recognized early on the need to develop critical masses within neuroscience, and as department chair, I had some influence over the areas chosen. As a result, there are numerous faculty here with whom I maintain active collaborations, especially with Jason Maclean. Such local collaborations are new to me, and I very much enjoy them.

Ray Guillery

As I was drafting this section, Ray Guillery died after a brief illness on April 7, 2017.[3] He was my most important mentor, colleague, collaborator, and friend. Our relationship spanned most of my life. I was heartened but not surprised at the vast number of people who expressed sadness and loss at his passing. I'll end this before getting too maudlin.

My work has benefited enormously from collaboration with Ray Guillery that spanned most of my scientific career (Ray, by the way, was short for Rainer, and it always irritated him when someone decided to be more formal with him and called him "Raymond"). I always thought of Ray

[3] Society for Neuroscience, "Member Obituaries: Rainer W. Guillery," http://www.sfn.org/MemberCenter/Member-Obituaries/GM/Ranier-W-Guillery.

Ray Guillery and me in front of the "Bean" in Chicago.

as my mentor, and many people seem surprised when I tell them that Ray was not my predoctoral or postdoctoral advisor. Ray always treated me as an equal. This collaboration has served me particularly well: It has made my scientific efforts far more interesting, fun, and significant. Indeed, I don't believe the SfN would have asked me to write this memoir were it not for my interactions with Ray. I think it best to emphasize and describe this before relating in any detail what sort of science issues dominated thinking in my laboratory, because these largely reflect my interactions with Ray.

I first met Ray in 1968. This was the same year I met my future wife, and in both cases the meetings led to a long and fruitful partnership. Ray then was a professor at the University of Wisconsin and I was still a graduate student at Penn. We hit it off immediately and began a long correspondence that started with snail mail and now is mainly represented by thousands of e-mails. Most of the correspondence is about neuroscience, but some is rather naughty gossip that is best kept private.

I was quite impressed that a senior, already famous neuroscientist could take a mere graduate student so seriously, and that reflects well on Ray, who has a pretty independent view of what is interesting scientifically. Our collaboration started off relatively slowly, but we hit on questions of mutual interest in visual development of cats that led to three coauthored research papers in the mid-1970s (Sherman et al. 1974; Sherman et al. 1975b; Sherman and Guillery 1976). Our collaboration moved onto a more theoretical plane in the early 1980s and received a boost when I spent a year-long sabbatical in 1985–1986 with Ray at Oxford University (he had moved there in 1984 to become chair of Human Anatomy). This sabbatical involved rather intense discussions on various aspects of the nature of the thalamus and thalamocortical relationships. Often these were arguments that led to one of us changing the view of the other as our different perspectives began to blend. Often one of us would offer an out-of-the box idea that the other tried to shoot down during further discussion. Often the shots hit their targets,

but occasionally such ideas survived our early skepticism to become more fully developed as hypotheses we used to challenge conventional wisdom regarding thalamus and thalamocortical relationships. Starting in 1986, we began to put down our thoughts on paper, and published 11 reviews or opinion pieces (Sherman and Guillery 1996, 1998, 2002, 2004a, 2004b, 2011, 2014; Guillery and Sherman, 2002a, 2002b, 2011) and three books (Sherman and Guillery 2001, 2006, 2013).

Ray and I made several attempts to get faculty positions at the same place. The first attempt was soon after I arrived back in America: Ray had arranged for me to visit his Department of Anatomy at Wisconsin to explore a possible position there. Unfortunately, the timing was bad, because Ray was away in London on sabbatical, and his chair, who was not enthusiastic about further development of neuroanatomy in his department, pretty much nipped this idea in the bud. Ray was pretty furious about all of this, feeling he was stabbed in the back. I soon ended up at the University of Virginia. When it became clear to me that Virginia would not be a place likely to develop neuroscience significantly and to Ray that Wisconsin was also decreasingly suitable for him, we looked at three other places more or less together: the University of California at San Francisco, the University of Utah, and the University of Chicago. The problem was that we each had criteria to be met, and satisfying both of us turned out to be too challenging. The offer I received at University of California at San Francisco represented a pay cut, because I was told that UCSF was so wonderful that I should jump at the opportunity to move there and not worry so much about salary. That did not sit well with me. As for Utah, my wife and I were already worried about raising our children in a setting dominated by religion (although Charlottesville was fine, the surrounding area was in the realm of the Moral Majority, which was housed in Lynchburg, just down the road from Charlottesville), and Utah did at the time seem dominated by religious tenets. Ray did end up at Chicago, but my wife and I were simply loath to raise our young family in any inner city at that time, and so I made my move to the bucolic environs of Stony Brook.

Together, Ray and I developed three major ideas that, we believed, challenge current views of thalamocortical processing (details to follow): glutamatergic pathways are inhomogeneous and can be classified into at least two types that we named *driver* and *modulator*; based on their driver input, thalamic relays can be divided into *first* and *higher order*, the latter representing a link in transthalamic corticocortical processing; and driver inputs to thalamus may play a role as efference copies.

My Predoctoral and Postdoctoral Trainees

In addition to being enormously lucky in my collaboration with Ray Guillery, I feel equally lucky with the quality of young scientists who spent time in my laboratory over the years. Table 1 lists them. It shows the general high

level of accomplishment they achieved as a group by noting their current or last known positions. I can claim little credit for their successes, because, as any of them would certainly testify, my role was mostly to offer support but to generally get out of the way of productive, energetic researchers who, as a group, deserve the vast bulk of credit for the reputation of the laboratory. I am very proud of them.

Research Perspectives

My research career has had one common theme, namely, understanding the circuitry of the thalamus and thalamocortical interactions, although there have been a few minor detours. I would rate my major research accomplishment overall as longevity and relative consistency in productivity rather than being able to boast of any special individual breakthroughs. It has been a career of steady but modest advances. I have also been very fortunate in my collaborators. My association with Ray Guillery has been described, but I must also emphasize the quality of the graduate students and postdoctoral fellows who worked in my laboratory over the years. These are listed in Table 1.

Two other themes have played a role in my thinking about the brain. One is that there is too much emphasis on cortex and a failure to take into account that many behaviors, some fairly complex, do not involve cortex at all. Even those that involve cortex succeed only if cortical outputs can play effectively through subcortical circuitry. That is, despite all the beautiful and complex circuitry of cortex, it would be pretty useless except for the fact that it can influence motor circuits in brainstem and spinal cord via its subcortical projections, specifically those from layer 5. The other theme is the importance of evolution in my thinking about brain organization. The two points are actually intimately related. My view of evolution, which is certainly not original with me, is that our early vertebrate ancestors, before cortex evolved, had complex behaviors subserved by brainstem and spinal pathways, and as cortex evolved, these subcortical circuits did not disappear to be replaced by newer cortical ones. Instead, these older circuits remain in our central nervous systems and operate independently or in partnership with corticofugal pathways to continue to control behavior. Another way of stating this is to point out that the evolution of cortex did not occur with the coevolution of a motor plant to which cortical circuitry is privileged; instead, cortex evolved outputs that affected the older motor circuits and had to do so in cooperation or competition with other, older brain areas to affect those same motor control areas.

It is my sense that, especially in the visual system, cortex has been overemphasized and thalamus ignored. This is perfectly exemplified by an experience I had about 30 years ago in London. The Museum of Natural History there had just announced a new exhibit involving the human brain, so I decided to stop by to see it. On entering the exhibit, I initially encountered a large three-dimensional model of the human visual system. In this model,

Table 1 Previous Trainees

Name	Where	Last Known Position	Location
Stephen Lehmkuhle	UVa	Chancellor	University of Minnesota (Rochester)
Michael Friedlander	UVa/USB	Executive Director	Va. Tech Carilion Research Institute
Stewart Bloomfield	USB	Professor and Associate Dean	SUNY College of Optometry
Mriganka Sur	USB	Professor & Chair	MIT
Lee Cox	USB	Professor & Chair	Michigan State University
William Guido	USB	Professor & Chair	Univ. Louisville Medical School
Alev Erişir	USB	Professor & Chair	University of Virginia
Kenneth Kratz	USB	Professor	LSU Medical School
Michael Loop	UVa	Professor	Univ. Alabama at Birmingham
Stuart Mangel	UVa	Professor	Ohio State University
†C.-S. Lin	UVa/USB	Professor	University of Mississippi
Nobuaki Tamamaki	USB	Professor	Kumamoto University (Japan)
Martha Bickford	USB	Professor	Univ. Louisville Medical School
Daniel Uhlrich	USB	Professor	Univ. Wisconsin Medical School
Dwayne Godwin	USB	Professor	Bowman-Gray Medical School
*James Wilson	UVa/USB	Professor	Emory University Medical School
*Rosalyn Weller	USB	Professor	Univ. Alabama at Birmingham
Roberto De Pasquale	UChi	Professor	Universidade de São Paulo
James Hamos	USB	Program Director	NSF
*Laurence Stanford	UVa/USB	Deputy Director	NIDA (NIH)
Allen Humphrey	USB	Associate Professor	Univ. Pittsburgh Medical School
Denis Raczkowski	USB	Assistant Professor	Duke University Medical School
C.-F. Hsiao	USB	Assistant Professor	University of Missouri
J.W. Vaughan	USB	Assistant Professor	Bowman-Gray Medical School
Penelope Murphy	USB	Assistant Professor	University of London
Daniel Llano	UChi	Associate Professor	University of Illinois
Charles Lee	UChi	Associate Professor	LSU Veterinary School
Brian Theyel	UChi	Assistant Professor	Brown University
Carmen Varela	USB/UChi	Postdoctoral Fellow	MIT
Elise Covic	UChi	Deputy Dean (College)	University of Chicago
Iraklis Petrof	UChi	Research Admin. Fellow	Children's Hospital of Philadelphia
Angela Viaene	UChi	Pathology Resident	University of Pennsylvania

*retired †deceased

(*continued*)

Table 1 Previous Trainees (Continued)

Name	Where	Last Known Position	Location
Current Laboratory Members			
Doreen Rhee	PhD Student		
A.J. Miller	PhD Student		
Minsu Yu	PhD Student		
Christina Mo	Postdoctoral Fellow		
Judy Prasad	Postdoctoral Fellow		
Briana Carroll	Postdoctoral Fellow		
Y.-W. Lam	Research Faculty		

the retina projected directly to the visual cortex. My snail mail correspondence with those responsible for the exhibit is another story (this is well before e-mail when people actually used the post office to communicate), but this model was eventually removed.

The various themes and their progression are described in the following sections, divided into periods defined by my various positions over the years.

While a Graduate Student at Penn

I started graduate school with Jim Sprague just at the time the Sprague Effect was described. Jim published his results in *Science* in 1966 (Sprague 1966). To my mind, this is a historically important paper, and rather than try my hand at summarizing it, I simply copy the abstract:

> Total contralateral hemianopia follows unilateral removal of the entire occipito-temporal neocortex in the cat. This deficit is classically ascribed to interruption of visual radiations serving cortical function ("cortical blindness") and is considered permanent. Return of vision to the hemianopic field after subsequent removal of the superior colliculus contralateral to the cortical lesion demonstrates that neither assumption is correct. The initial hemianopia is apparently due to depression of function of the colliculus ipsilateral to the cortical lesion, a depression maintained by influx of inhibition from the crossed colliculus. Thus, removal of the contralateral tectum, or splitting of the collicular commissure, abolishes this inhibition and allows the return of function in the ipsilateral colliculus, and with it the recovery from hemianopia. These findings emphasize that visually guided behavior is mediated at both cortical and midbrain levels, and that there is a marked interaction between these sites. (Sprague 1966)

In essence, this says that much visually guided behavior can be performed in the absence of cortex. The initial observation that cortical lesions cause apparent blindness continues to be misinterpreted to mean that cortex is pretty much the end-all and be-all for vision, but this and subsequent work (Wallace et al. 1990; Ciaramitaro et al. 1997) make clear that such blindness is due partly to the secondary effects of the cortical lesions that somewhat denervate and thus incapacitate critical subcortical sites, such as the superior colliculus. Note that the recovery of vision that the Sprague Effect documented following collicular manipulation was supported by subcortical structures that are themselves damaged because of the removal of cortical input. Thus, the role in vision of such structures as the superior colliculus in normal, intact animals may be even greater than that noted by the Sprague Effect.

What I find surprising is that this seminal (to me) observation seems lost in history. During the past few SfN meetings, I have noticed posters describing experiments that are eerily similar to or complement the Sprague Effect, but each time I have asked the presenter (invariably a graduate student or postdoctoral fellow) if he/she has ever heard of Jim Sprague or the Sprague Effect, I have been greeted with blank stares. I suppose sometimes it's easier to repeat classical experiments than to comb through the literature.

In any case, the Sprague Effect was one of the earliest scientific discoveries I was exposed to, and it clearly had an impact on me. Ever since, I championed the idea that many behaviors have a significant subcortical substrate, a view that has been consistently ignored. I often took the notion too far, relegating cortex too much. Nonetheless, this philosophical bias has stayed with me. I regard this as perhaps the main scientific point of view I absorbed while a graduate student.

While a Postdoctoral Fellow in Australia

Two different research questions began to emerge as a carryover from my graduate experience as I started my postdoctoral stint, and eventually they more or less coalesced. First, I rather passively allowed myself to be recruited into ongoing projects at the beginning of my time in Canberra. This suited my subcortical bias, because the initial experiments with Ken Sanderson involved mapping of the lateral geniculate nucleus, and my later collaboration with Jonathan Stone and Peter Hoffmann also involved the lateral geniculate nucleus. Second, like many of my generation, I became fascinated with and affected by the science of Hubel and Wiesel, especially their work on the critical period.

I joined the experiments on X and Y cells with Jonathan and Peter, which started a research line that formed the basis of my efforts for the next several decades. I was a bit of a latecomer to this effort. This was transformative for me, because prior to this, I was in search of research themes that could start to define my career, and these experiments provided me with exactly what I needed to develop a sustainable research approach.

Part of my reason for wanting to join Jonathan and Peter had to do with a hunch related to visual development. That is, Hubel and Wiesel showed that visual deprivation by early lid suture in cats led to severe loss of input to cortical cells from the deprived eyes (Wiesel and Hubel 1963b, 1965). They also reported "normal" responses among geniculate cells in these cats despite finding that these same deprived geniculate cells were anatomically shrunken (Wiesel and Hubel 1963a). I found the incongruity between the anatomy and physiology of geniculate cells odd and thought that perhaps a cell type was selectively affected and shrunken, leaving other cell types with normal properties. Testing the possibility of differential deprivation effects on geniculate X and Y cells seemed like a logical next step, and this fit perfectly with the sort of experiments Jonathan and Peter had planned. They accepted the hypothesis as reasonable, and so in addition to studying geniculate X and Y cells in normal cats, we also did so in visually deprived animals.

The result served as the basis for a great deal of my future research (Sherman et al., 1972). Much of this had to do with studies of binocular competition during development, often in collaboration with Ray Guillery. Here, the concept of binocular competition bears some explanation. The extreme nasal retina sees peripheral visual field that is beyond the image formed on the other eye's temporal retina, and so this segment of visual field is seen by only one eye: This is the monocular segment, and the central, majority of visual field is the binocular segment. The representations of these segments in central visual structures, such as the lateral geniculate nucleus and visual cortex, are known as the binocular and monocular segments of those regions. The idea of binocular competition during development is that circuits from the two eyes compete for control of neural connections and, with normal development, a balance is struck. However, during development under visual deprivation, circuits related to the deprived eye are at a competitive disadvantage because of the deprivation, allowing the nondeprived eye's circuits to dominate. However, this happens only in the binocular segment, where competition can occur, because circuits mapped to the deprived monocular segment by definition do not suffer from a competitive disadvantage. Thus, the deprived monocular segment can develop relatively normal connectivity.

Getting back to my studies with Jonathan and Peter of geniculate X and Y cells, we found that, in cats reared with monocular deprivation, X cells in deprived geniculate layers were normal but that there was a drastic loss of Y cells. Furthermore, the Y-cell loss was limited to the deprived binocular segment, echoing a result from Ray Guillery's laboratory that geniculate cell shrinkage from monocular deprivation was limited to the binocular segment (Guillery and Stelzner 1970). In both instances, Y cell loss and cell size, the deleterious effects of deprivation were limited to the binocular segment, observations that helped to establish binocular competition as a major mechanism for visual development.

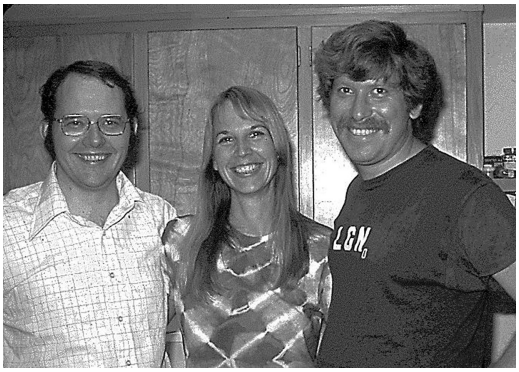
Our finding of Y cell loss never had the impact I thought it should, which I suppose is a complaint common to many scientists, founded or otherwise. My view is that there are two related reasons for this. One is the cortico-centric bias of the field. The idea that interesting deprivation effects could have a partial subcortical basis was hard for cortical chauvinists to accept. Related to this was the suggestion that the observation of a Y cell loss was some sort of sampling artifact. That is, Y cells were shrunken and thus harder to isolate for recording, as if even this explanation made sense: Why would one expect shrunken cells to be normal? While this result of failure to record normal numbers of deprived geniculate cells may still be open to interpretation, I believe that subsequent results point pretty clearly to deprivation affecting Y cells considerably more than X cells (Friedlander et al. 1982; Sur et al. 1982; Sur et al. 1988).

A final research direction I started in Australia was to apply the perimetry approach in cats that Jim Sprague used to define the Sprague Effect. Basically, this perimetry technique determined in which parts of the visual world a cat could detect the appearance of a novel target. I used perimetry testing to evaluate the effects of visual deprivation on this detection behavior. Perimetry testing of cats formed another theme, along with visual deprivation and parallel processing, that I carried from Australia to my next academic destination.

While a Faculty Member at Virginia

Perimetry Testing: The perimetry testing of cats that I carried over from Australia had two related goals. The lesser goal was to extend the Sprague Effect to normally reared cats with cortical and midbrain lesions, whereas the more important (to me) goal was to use this extension as control data for technically similar studies of visually deprived cats. The deprivation experiments had two main findings. First, monocularly deprived cats had normal vision for stimulus detection in the deprived monocular segment, which provided a behavioral correlate to the finding of normal geniculate cell sizes and Y cell presence in the deprived monocular segment (Sherman 1973). Second, the asymmetry between perimetry in the two eyes of monocularly deprived cats (i.e., the nondeprived eye had normal perimetry, whereas the deprived eye was blind except for the monocular segment) disappeared after visual cortical lesions, and after such lesions, normally reared and visually deprived cats exhibited the same perimetry behavior, which also means that the cortical lesion actually *improved* vision for the deprived eye (Sherman 1974). This latter result indicates that perimetry defects associated with early visual deprivation had neuronal substrates largely limited to geniculocortical circuitry and that retinotectal circuits developed normally during deprivation.

A Key Early Collaboration with Tom Norton and Vivien Casagrande: Here again, I note the loss of one of my best friends and key collaborators in



Tom, Vivien and me at Duke in 1977.

neuroscience: Vivien passed away at the end of 2016. Like my relationship with Ray Guillery, mine with Viv was long lasting and enduring. We first met in 1972 just after I returned from Australia, and we remained close ever since. Viv was one of the most remarkable women I ever met: She was generous, dedicated, loyal, and talented, and she packaged all of this with a great sense of humor. I along with all of her colleagues miss her greatly.

Early in my stint as a University of Virginia faculty member, I collaborated on experiments carried out at Duke University with Tom Norton and Vivien Casagrande. Tom was a faculty member there and served as our host; Viv and I commuted for the experiments, she from her position as a postdoctoral fellow with Ray Guillery at the University of Wisconsin. My commutes involved horrid bus trips from Charlottesville to Durham. The main purpose of these experiments was to determine whether the X/Y concept of parallel processing could be extended to species other than the cat. The species we chose for this was the tree shrew, because it seemed an important species from the point of view of evolution of mammalian vision and is a species that Vivien had worked on extensively as a graduate student with Irving Diamond at Duke.

There was a clear scientific yield of this collaboration: The identification of X and Y cells in the tree shrew's lateral geniculate nucleus as well as loss of geniculate Y cells in visually deprived tree shrews (Sherman et al. 1975a; Norton et al. 1977). But for me, there were two other less easy-to-measure benefits. First, working with Tom and Vivien, despite the appalling hours of all-night experiments, was sheer fun. I also enjoyed my experiences as a graduate student in Philadelphia and postdoctoral fellow in Canberra, but those environments were created by my mentors there, and this was my first experience with an environment I created with my close peers. This gave me confidence that my ongoing career would continue to be fun, if nothing else. The other benefit came from my interactions with Vivien. Her approach to neuroscience was driven by principles of evolution. Before this, evolution was

an abstract notion for me that played little or no role in my neuroscientific thought; since this interaction with Vivien, I have shared her perspective on evolution, and it has definitely shaped my thinking, for better or worse.

A Key Early Collaboration with Ray Guillery: Another collaboration early in my faculty stint at the University of Virginia was with Ray Guillery. During this early period of my time at the University of Virginia, our efforts together moved from somewhat-casual discussions to a more formal and productive level. The catalyst for this was our shared interest in the concept of binocular competition as a major mechanism of visual development as described earlier. This started with Ray's demonstration noted previously of normal geniculate cell sizes in the deprived monocular segment (Guillery and Stelzner 1970), and he followed this up with his ingenious artificial monocular segment model—that is, he sutured one eye of a kitten and simultaneously made a small lesion in the central temporal retina of the open eye. This lesion created an artificial monocular region (which he called the "critical segment") mapped to the deprived eye, and Ray demonstrated that deprived geniculate cells grew to normal size in the deprived geniculate region mapped to the artificial monocular segment (Guillery 1972). This crucial supplement to the earlier observations more firmly established that the relevant factor in visual development is binocular competition and not some property of peripherally versus centrally mapped regions of the visual pathways. Once this initial observation was made, Ray and I extended it by testing the artificial monocular segment model for other evidence of binocular competition. Thus, we showed that in both natural monocular and artificial monocular segments there was normal development of geniculate Y cells, normal responses of cortical cells to visual stimuli, and normal location of objects in perimetry testing (Sherman et al. 1974; Sherman et al. 1975b).

Further Visual Deprivation Studies: Most of the rest of the research effort of my Virginia laboratory was devoted to studies of the effects of visual deprivation on the central visual pathways and visual behavior of cats. Much of this may be seen as a failed effort to convince the field that there were effects of deprivation outside of those described in visual cortex. However, there was one finding we reported that I believe is critical to this issue and that has not received much attention. The basic finding was that visually deprived cats had much poorer visual capabilities than did normally reared cats with bilateral lesions of visual cortex (areas 17 and 18) (Lehmkuhle et al. 1982; Lehmkuhle et al. 1984). Our conclusion can be appreciated by our final summary point in one of the papers:

> Finally, because the amblyopia of normally reared cats with lesions of striate cortex is far less severe than that of the lid-sutured and dark-reared cats, it follows that the constellation of deficits

> reported for striate cortex in these visually deprived cats cannot provide an adequate neural explanation for their amblyopia. Attempts to relate deprivation amblyopia to striate cortex abnormalities should thus be reconsidered. (Lehmkuhle et al. 1982)

Sticking and Staining: A final research line that started toward the end of my tenure at Virginia and carried over through my move to Stony Brook was the technique of labeling physiologically identified neurons recorded intracellularly with a dye that enabled post hoc morphological reconstruction of the same cell, also known as "stick-and-stain." Although this approach had been used successfully for some time in invertebrate preparations with large and accessible neurons, it was a paper that accomplished this approach with cat caudate cells (Kitai et al. 1976) that really caught my attention. However, this seemed like hopeful pie-in-the sky to me until the arrival of a very talented postdoctoral fellow in my laboratory, namely, Mike Friedlander. Mike never saw a challenge he feared to attack and immediately agreed that it would be a good thing to adopt this approach to study the structure–function relationships of geniculate X and Y relay cells and interneurons in the cat. So we did, largely through Mike's ability to make it all work (Friedlander et al. 1979, 1981; Friedlander and Sherman 1981).

This was the start of a series of studies that investigated the different functional organization of these parallel pathways, and it benefited in the beginning by the addition of Larry Stanford, another postdoctoral fellow committed to these studies. We continued such studies after the move of the laboratory to Stony Brook in 1979, a move that was greatly supported by the fact that Mike and Larry made the move with me, and it was the two of them who did the bulk of the work reestablishing the laboratory.

While a Faculty Member at Stony Brook

More Sticking and Staining: We immediately began extending the stick and stain approach in several ways. We added W cells to the mix (Stanford et al. 1981); we described the morphology of both retinogeniculate and geniculocortical X and Y axons (Sur and Sherman 1982; Humphrey et al. 1985a; Humphrey et al. 1985b); we succeeded in taking this analysis to the electron microscope level (Wilson et al. 1984; Hamos et al. 1985; Hamos et al. 1987); and we also applied this approach to the study of visual deprivation and development, providing further evidence for selective deprivation effects on the Y system (Friedlander et al. 1982; Sur et al. 1982; Sur et al. 1984). All of this provided what I would describe as useful insight into the differential functional organization of the parallel pathways in the cat visual system, details of which can be found in the cited publications.

Through the 1980s, there was considerable, sustained interest in parallel processing, especially after the concept successfully extended to

primates, where the cat's W/X/Y streams appear respectively homologous to the monkey's K/P/M equivalents (reflecting inputs through the geniculate koniocellular, parvocellular, and magnocellular layers). Parallel processing remains as important as ever, but for reasons that elude me, interest in this topic has all but evaporated from mainstream questions regarding the organization of visual pathways.

Details of Geniculate Circuitry: The extension of structure–function relationships to the electron microscope level encouraged us to continue using mainly morphological techniques to dig deeper into the functional circuitry of the cat's lateral geniculate nucleus. Key to this was a very talented and long-serving technician, Sue Van Horn, who coauthored many of the resultant publications; a graduate student Alev Erişir; and two postdoctoral fellows, Jim Hamos and Martha Bickford. This led to a certain amount of new understanding, most details of which are beyond the scope of this writing, but included X/Y differences, the location of synapses onto dendritic trees of relay cells, the organization of triadic circuitry in glomeruli, and details of circuits involving GABAergic interneurons.

One surprise was our finding from a detailed analysis of inputs to geniculate relay cells. In spite of the fact that we've known for decades that the main information relayed to cortex by these cells is carried by the retinal input, we concluded that retinal synapses represent only about 5 percent of all synapses onto relay cells (Van Horn et al. 2000), which lowered this estimate from the earlier one of 15–20 percent proposed by Ray Guillery (1969). This has implications for our ideas about "drivers" and "modulators" expressed in the following sections.

Tonic and Burst Firing: Much as the report of intracellular staining of basal ganglia cells (Kitai et al. 1976) inspired us to try this approach for geniculate cells in the cat, back-to-back papers from the laboratory of Rodolfo Llinás (Jahnsen and Llinás 1984a, 1984b) caught our attention. I thought the idea that thalamic relay cells had different firing modes controlled simply by their background membrane voltage offered exciting new possibilities for control of thalamocortical transmission. This thinking was further supported by an influential idea—the "searchlight hypothesis"—proposed by Francis Crick (1984) that suggested that these firing modes underlie key attentional mechanisms. We thus decided to explore the possible functional significance of these firing modes.

Several students and postdoctoral fellows were key to our progress here, most notably Bill Guido. We provided three main advances: We showed how the different firing modes could be identified in extracellular recording, we showed some of the neuronal circuitry that seemed effective in controlling which firing mode presented at any given time, and we suggested a role for the firing modes (Guido et al. 1995; Sherman 1996).

We found that tonic firing offered a more linear relay of information, and so information relayed during tonic firing would not suffer the nonlinear distortions imposed by burst firing; thus, tonic firing would be better for stimulus discrimination. However, the nonlinearities seen during burst firing would enhance signal-to-noise ratios; thus, burst firing would be better for stimulus detection and could serve as a "wake-up call" to cortex that a new stimulus has appeared.

This idea turned out to be quite controversial because of the prevailing view that burst firing occurred only during sleep or epilepsy and was not an effective relay mode: Tonic firing was the only mode employed during normal waking behavior. That is, the hypothesis that burst and tonic firing both provided different advantages for thalamic relays during waking behavior requires that both firing modes, and not just tonic firing, be present during such behavior. The strongest advocate against our idea of a useful relay function for burst firing was the late Mircea Steriade, who insisted that bursting never occurred during waking behavior (e.g., Steriade 2001). Mircea was a remarkably productive scientist who made many seminal contributions to thalamocortical processing. In this case, however, his stubborn intransigence baffled and frustrated me, because there was ample evidence then and contemporary evidence still being produced that makes pretty clear that bursting does occur during waking behavior in a number of different species and systems tested. Furthermore, many of these studies provide evidence for the "wake-up call" hypothesis for burst firing (for a few examples, see Fanselow et al. 2001; Swadlow et al. 2002; Lesica and Stanley 2004; Ramcharan et al. 2005; Lesica et al. 2006; Andolina et al. 2013; Ortuno et al. 2014; Hu and Agmon 2016; Whitmire et al. 2017). The issue of burst and tonic firing in thalamic relay cells remains an important topic that needs to be better understood.

First and Higher Order Thalamic Relays, Drivers, and Modulators: Following my 1985–1986 sabbatical in Oxford with Ray Guillery, we started in earnest to discuss and argue about general issues regarding thalamocortical relationships. It took some time for us to realize that our discussions could be productively developed into publications, first with reviews and finally with monographs. Two themes took shape in this way in the 1990s: the concepts both of first and higher order thalamic relays as well as of driver and modulator classes of glutamatergic afferents.

Ray wrote a 1995 review that for the first time proposed that thalamic relays could be divided into first and higher order, the former relaying a subcortical input (e.g., retinal input for the lateral geniculate nucleus) and the latter, an input from layer 5 of a given cortical area as a link in a transthalamic corticocortical information route (Guillery 1995). In our review that followed soon after (Sherman and Guillery 1996), we extended this idea and made it a central theme of our further collaborative work.

The driver/modulator distinction for glutamatergic inputs evolved from two perspectives. First, there was a prevailing view that saw information processing as involving glutamatergic pathways to carry the information, with other pathways (e.g., cholinergic, noradrenergic, and GABAergic) playing a more subtle modulatory role by affecting how glutamatergic pathways were processed. This, in turn, suggests a more or less homogeneous function for glutamatergic afferents, with them acting in some sort of anatomical democracy to affect or control their targets—that is, the larger the input, the more powerful it must be. However, our knowledge of geniculate circuitry belied this view, because the two prominent glutamatergic inputs onto relay cells, inputs from retina and layer 6 of visual cortex, did not follow these rules. This is because these inputs clearly seemed quite different, and only the retinal input appeared to carry the basic information to be relayed. This made the retinal input the more prominent in driving geniculate relay cells, and yet it has a much smaller anatomical footprint with only about 5 percent of the input synapses versus about 40–50 percent for the cortical input.

We struggled with this until a paper appeared from David McCormick's laboratory showing that corticogeniculate input activates metabotropic glutamate receptors, as well as ionotropic ones, but retinal input activates only ionotropic receptors (McCormick and Von Krosigk 1992). This is another example of a paper triggering a new approach both in the development of ideas with Ray as well as the design of experiments in my lab. Ray and I started to look for and find more general patterns associated with different kinds of glutamatergic input, focusing initially on what we knew of thalamic circuitry. We realized that these different patterns could be a basis for a straightforward classification of glutamatergic synapses. Following this notion, we concluded that these synapses could be divided into two quite different classes, which we called *drivers* and *modulators*, and we listed a number of parameters that could be used to distinguish them. Eventually, we published this perspective (Sherman and Guillery 1998). We tried to put it all together in a monograph, our first of three (Sherman and Guillery 2001). We continued to refine and expand our ideas in a series of reviews and thought pieces (Sherman and Guillery, 2002, 2004a, 2004b; Guillery and Sherman 2002a, 2002b), culminating in our last two monographs (Sherman and Guillery 2006, 2013).

After Ray and I established fairly clear hypotheses regarding first and higher order thalamic relays and drivers and modulators, my laboratory began an experimental plan designed to test these ideas. This was started at the end of my tenure at Stony Brook via a PhD thesis by my graduate student, Iva Reichova. She slightly adapted the mouse thalamocortical slice preparation pioneered by Ariel Agmon and Barry Connors (Agmon and Connors 1991) to demonstrate that the layer 5 input from barrel cortex (primary sensory cortex, or S1) to the posterior medial nucleus, a higher order thalamic relay, exhibits driver characteristics, just like retinogeniculate synapses, whereas layer 6 corticothalamic synapses show modulator

properties (Reichova and Sherman 2004). This study also established a number of criteria to distinguish drivers from modulators; chief among them was the short-term plasticity—depression for drivers versus facilitation for modulators—and activation of both ionotropic and metabotropic glutamate receptors by modulators but only ionotropic receptors by drivers.

After its move to Chicago, my laboratory continued this research line as its main theme.

While a Faculty Member at Chicago

Transthalamic Pathways: The presence of transthalamic pathways (i.e., cortico-thalamo-cortical pathways involving higher order thalamic relays) has been a major theme of our work in Chicago. The clearest example of such a pathway was provided by two talented members of my laboratory: Brian Theyel, an MD-PhD student, and Dan Llano, a postdoctoral fellow who had been an MD-PhD student and just finished a residency in neurology. In brain slices from the mouse, they clearly demonstrated a transthalamic pathway from S1 through the posterior medial nucleus to S2 (Theyel et al. 2010). We also provided evidence for transthalamic pathways in the visual and somatosensory systems.

Based on these examples, there seemed to be a pattern: When a direct corticocortical connection exists (e.g., S1 to S2), there is also a transthalamic one (e.g., S1 to the posterior medial nucleus to S2). Currently, we are working to extend this to cortical areas beyond purely sensory ones. A good start beyond purely sensory circuits has been the work of a current postdoctoral fellow, Christina Mo, who has just demonstrated parallel direct and transthalamic pathways between S1 and the primary motor cortex, the transthalamic pathway involving the posterior medial nucleus.

This work has raised a number of questions we are currently focused on: How common is the pattern of parallel direct and transthalamic connections between cortical areas, or, how commonly are cortical areas connected by only one or the other? What is different in the information carried by each route? Why is one of these circuits relayed by thalamus?

Drivers and Modulators: Our work on drivers and modulators followed three main themes. One was to demonstrate the significance of this classification, another was to extend the classification from thalamus to cortex, and the last was to gain some understanding of the function of modulatory inputs. Regarding the last point, our hypothesis is that driver inputs carry the main information for circuits to work on, whereas the modulators affect how driver information is processed, much like the classical modulatory inputs (e.g., cholinergic, serotonergic, etc.). A key to all of these modulatory synapses is that they commonly activate metabotropic receptors; for instance, cholinergic inputs typically activate muscarinic receptors, which

are metabotropic, and, as noted, the glutamatergic modulatory inputs activate metabotropic glutamate receptors. Activation of metabotropic receptors seems to be a key factor in providing modulatory functions for all of these inputs. However, a difference between classical versus glutamatergic modulatory systems is that the former is relatively diffusely organized and relates to overall behavioral stages, such as level of alertness, whereas glutamatergic modulators are the only ones with precise topography, which is needed for many processes such as spatial attention, adaptation, and so on.

I'm afraid at this point we may have introduced some terminological confusion to the subject. That is, I was concerned that our use of the terms "driver" and "modulator" suggested their functions—information bearing for driver and modulatory for modulator—a terminological approach that I have criticized earlier to favor "X" and "Y" as terms over "sustained" and "transient." The driver/modulator functional hypothesis, while plausible and attractive, remains unproven. Therefore, we started calling these glutamatergic inputs "Class 1" (driver) and "Class 2" (modulator). I received some criticism for this, because the Class 1 and 2 terms confused people. So I've become inconsistent, going back and forth a bit: mea culpa. For clarity, I'll stick to "driver" and "modulator" in the remainder of this piece, with the important proviso that the evocative functions for these classes remain a hypothesis.

An example of the importance of the classification is work first carried out mainly by Charles Lee, another postdoctoral fellow in my laboratory, who identified the properties of the glutamatergic inputs from the inferior colliculus to both the ventral and dorsal divisions of the medial geniculate nucleus (first and higher order, respectively). Conventional wisdom at the time held that these inputs represented links in parallel information streams through thalamus to cortex. Charles, however, showed that while input to the ventral division was all driver, and hence a likely information route, input to the dorsal division was all modulator, and so, instead of a parallel information route, the pathway to the dorsal division seems more likely to modulate the transthalamic pathway—that is, the pathway from primary auditory cortex through the dorsal division of the medial geniculate nucleus to the second auditory area (Lee and Sherman 2010). Thus, applying the driver/modulator classification changes rather dramatically the perspective of the functional organization of this part of the ascending auditory system.

Quite recently, work from a graduate student (Angela Viaene) and two postdoctoral fellows (Christina Mo and Iraklis Petrof) in my laboratory extended this analysis to the somatosensory inputs to thalamus in the mouse (Mo et al. 2017). (Angela and Iraklis formed quite a productive team in the laboratory, and furthermore joined together in matrimony and, recently, parenthood.) Here, the conventional view is that there are parallel information routes to cortex, the lemniscal one involving medial lemniscal input to the ventral posterior medial nucleus to S1, and the paralemniscal one involving input from the spinal nucleus of the fifth nerve to the posterior

medial nucleus to S2. Although the lemniscal pathway is all driver, the paralemniscal input to thalamus is mostly modulatory, again suggesting that the conventional view needs rethinking.

Much of our effort has been devoted to extending the classification of glutamatergic pathways from thalamic circuits to cortical ones. Three postdoctoral fellows (Charles Lee, Roberto DePasquale, and Iraklis Petrof), a graduate student (Elise Covic), and an MD-PhD student (Angela Viaene) were critical to this effort (Lee and Sherman 2008, 2009; Covic and Sherman 2011; DePasquale and Sherman 2011; Viaene et al., 2011a, 2011b, 2011c; Lee and Sherman 2012; Petrof et al. 2015). Our expectation was that, when we investigated the more complex circuitry of cortex, we would identify classes in addition to drivers and modulators. We found instead that all glutamatergic pathways we could identify, both thalamocortical and corticocortical, easily fit into the driver or modulator category. However, we did find that driver pathways in cortex could further be divided into three subtypes. It now appears to us that there are two basic types of synaptic input seen in thalamus and cortex—the types we have identified as driver and modulator—and that the properties of each in thalamus mirror those in cortex.

Ideas Regarding Efference Copies: The final conceptual development from Ray and me relates to the speculative relationship between driver inputs to thalamus (i.e., the input relayed to cortex) and efference copies. Efference copies, also known as corollary discharges, are an essential feature of neuronal processing for any creature with complex behavior, because they enable the animal to disambiguate events in the environment from apparent environmental changes caused by the animal's own behavior. A good example is eye movements: Every time we move our eyes, and we make roughly three saccades per second, the visual image of the outside world moves in the opposite direction on our retinas. Yet we don't perceive the visual world as unstably spinning about—it remains stable. This is because a copy of the command to move the eyes is fed back into the visual processing stream so that the effects of the motion can be subtracted from our visual perception.

As I recall, the evolution of the ideas Ray and I developed on this subject was as follows. We were engaged in long-standing discussions about transthalamic pathways, and particularly the layer 5 parts of the circuits, when we belatedly had our attention drawn to a series of papers from the laboratory of Martin Deschênes, papers that described the morphology of layer 5 corticofugal exons from several cortical areas (Deschênes et al. 1994; Bourassa and Deschênes 1995; Bourassa et al. 1995; Levesque et al. 1996). Those axons that innervated thalamus as the first stage in transthalamic circuits all branched, some quite heavily, to innervate numerous other subcortical structures. This reminded me of an earlier study from my laboratory showing that all labeled retinogeniculate axons in the cat branched to innervate midbrain structures as well (Tamamaki et al. 1995).

Ray and I started to generalize and speculate. It seemed that many, and perhaps all, driver inputs to thalamus arrived via branching axons. This seems to be a clear anatomical fact for the relatively few examples that have been documented, but what does it mean? We struggled to come up with an explanation. One aspect of branching axons that seems clear is that this is arguably the most efficient and foolproof means of delivering exactly the same message, or more precisely, the same temporal pattern of action potentials, down all branches to multiple targets. This does not mean that all targets respond identically, because synaptic differences play a role here, but if the goal is to send multiple copies of a message from one neuron to many, using branching axons seems the best solution.

Thus, we reasoned, the message sent to thalamus for relay to cortex was in many cases, if not most or all cases, a copy of messages sent to multiple other subcortical targets. When we looked through the literature regarding these extrathalamic targets of these branched axons, lightbulbs went off: Many of these targets appear to be motor control centers, such as bulbospinal centers, and some of these layer 5 axons that branch to innervate thalamus are corticospinal neurons, directly innervating spinal circuits via these extrathalamic branches. Indeed, these layer 5 projections represent the one and only means for cortex to influence behavior by targeting older motor centers, and so these connections are plausibly considered to be motor messages or commands sent from cortex. It thus follows that the branches of these axons that target thalamus carry copies of the motor commands: This is a nice definition of an efference copy. It also follows that if cortex sends out motor commands via layer 5 corticofugal cells, which is the only known pathway for cortex to influence behavior, it logically follows that these commands must be accompanied by efference copies sent back into cortical processing centers involved with those commands. The branching of layer 5 corticothalamic axons provides a plausible neuronal substrate for this, and it is hard to imagine other likely pathways for such efference copies of *cortical* motor commands. Ray and I have written extensively about this—further details can be found there—and this remains an idea I hope to continue to develop, one that now dominates much of the thinking in my laboratory to design experimental tests of these ideas.

Coda

Writing this piece has been a real pleasure for me. I haven't previously taken much time to ponder where I am in my life and how I got here, and preparing this brief autobiography has forced me to do so. It's an exercise I recommend to everyone.

I've had a very successful and rewarding life and career as judged by the only arbiter who counts—me. How others view this is frankly of less concern to me. But in recollecting how I arrived at this point in my journey, I've

come to appreciate how much blind but good luck has determined my fate. It is certainly humbling to come to appreciate just how much factors over which one has no control play in one's ultimate fate. In my case, I have been extraordinarily lucky, something I have tried to document here.

My luck has been expressed both in terms of random incidents and people with whom I've interacted and collaborated. The two most important people have been my wife Marjorie and Ray Guillery. Interestingly, I met both the same year, 1968, and in each case that was the start of an ongoing and very successful collaboration. I am also very proud of the fact that most of the predoctoral and postdoctoral students who have passed through my laboratory went on to very successful scientific careers (see Table 1), which is more a testimony to my good luck in attracting them than any pixie dust I covered them with—indeed, it was their productivity in my laboratory that is the chief factor in my own professional success.

I often wonder what path I'd choose if I were a student today and had the same interest in science I did when I was young. Would my fascination with science and research and the attraction of an academic career be a sufficient drive to take the path I took when younger? Or would my current knowledge of the difficulties involved with that path, especially the shortage of both appropriate academic positions and government (read, NIH) funding, deflect me toward less risky paths, like medical or business school? I'd like to think I would take the risk, because of the wonderful and fulfilling career academic science offers and also because I don't think I'd relish being a physician or businessman. I've tried to imagine what my answer would be, but I really don't know.

But that's all speculation, and the fact is that I've enjoyed a wonderful, fulfilling career. On reflection, it's clear that, during my time in the field, neuroscience has made remarkable advances, and I feel good about playing some part in that. I have no plans to retire, because why should I stop doing what I enjoy so much? It's as if I'm being paid rather handsomely for a hobby I'm passionate about. And I'm just as excited about the research ongoing in my laboratory as I ever was.

The trip has been well worth it.

Acknowledgments

I thank the following for offering useful advice on various drafts of this manuscript: Ruth Anne Eatock, Elizabeth Grove, Jason MacLean, and Marjorie Sherman.

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