



The History of Neuroscience in Autobiography Volume 7

Edited by Larry R. Squire

Published by Society for Neuroscience

ISBN: 0-19-539613-8

Robert H. Wurtz

pp. 704–764

<https://doi.org/10.1093/acprof:oso/9780195396133.003.0016>



Robert H. Wurtz

BORN:

Saint Louis, Missouri
March 28, 1936

EDUCATION:

Oberlin College, A.B, Chemistry (1958)
University of Michigan, Ph.D., Physiological Psychology (1962)

APPOINTMENTS:

Research Fellow, Departments of Physiology and Neurology, Washington University School of Medicine (1962–1965)
Research Associate, Committee for Nuclear Information (1962–1963)
Research Fellow, National Institute of Neurological Diseases and Blindness, NIH (1965–1966)
Physiologist, National Institute of Mental Health, NIH (1966–1978)
Visiting Scientist, Physiological Laboratory, Cambridge University (1975–1976)
Founding Chief, Laboratory of Sensorimotor Research, National Eye Institute, NIH (1978–2002)
Chief, Section on Visual Motor Integration, Laboratory of Sensorimotor Research, NEI, NIH (2002–present)
NIH Distinguished Investigator (2008–present)

HONORS AND AWARDS (SELECTED):

W. Alden Spencer Award, Columbia University (1987)
National Academy of Sciences (1988)
American Academy of Arts and Sciences (1990)
President, Society for Neuroscience (1991)
Karl Spencer Lashley Award, American Philosophical Society (1995)
Friedenwald Award, Association for Research in Vision and Ophthalmology (1996)
Distinguished Scientific Contribution Award, American Psychological Association (1997)
Institute of Medicine of the National Academy of Sciences (1997)
Dan David Prize for the Future Time Dimension: “Brain Sciences” (2004)
Ralph W. Gerard Prize of the Society for Neuroscience (2006)
Honorary Doctor of Science, Oberlin College (2009)
Grass Lecture, Society for Neuroscience (2009)
Gruber Neuroscience Prize (2010)

Robert H. Wurtz developed methods for studying the visual system in awake behaving monkeys, a technique now widely used for the study of higher brain functions. He has pioneered the use of this technique to explore the neuronal basis of active vision, the integration of the visual, oculomotor, and cognitive functions underlying visual perception. He has done so in collaboration with a series of postdoctoral fellows, many of whom have gone on to become leaders in the field of systems neuroscience. His discoveries with these collaborators include establishing the functional organization of the primate superior colliculus, its role in generating saccadic eye movements, and its contribution to higher functions, including visual attention; the identification of a brain circuit for a corollary discharge of eye movements and the possible contribution of this corollary to stable visual perception; the circuit connecting the basal ganglia to the superior colliculus and the nature of its inhibitory action; the contribution of cortical visual motion processing to perception, pursuit eye movements, and the registration of large field optic flow. He was founding Chief of the Laboratory of Sensorimotor Research in the National Eye Institute of the National Institutes of Health.

Robert H. Wurtz

I try to write a scientific paper in a way that states a question, explains the methods to address it, gives the answer, and then discusses what it means. Like the biographical sketch above, it is a formal archival report. But both in the limited experiment and in the larger life, these reports give none of the real course of events. All the twists and turns of real science and a scientist's life are converted into a straight line from goal to achievement. In this autobiographical sketch I try to give the real why of experiments and of my life in doing the experiments.

My scientific life spans the rise of neuroscience as a scientific discipline with my own work dedicated to exploring systems within the brain. I hope my comments provide a little insight into the development of my nook of systems neuroscience. I also hope it might encourage younger scientists to realize that mistakes are not fatal, only failing to take the risks that can produce mistakes is fatal. Of course I am the main beneficiary of this autobiography because it provides a sobering summary of where so much time has gone so fast. I am grateful to Larry Squire for his very flattering invitation; I would never have done this otherwise.

The Beginning (1936–1954)

My father hated his job. I start my commentary with such a seemingly irrelevant statement because I think it shaped the course of my life in science. I was shaped somewhat by inherent abilities, but more by the circumstances in which I grew up. I now realize that none was more important than my family, teachers, and friends, and none of those rivals the influence of my father.

My father was born in Indianapolis, Indiana, in 1887 during a sojourn his father made for several years from St Louis. He was named Robert after his father, who was a tool and die maker designing the blades that slice the patterns into picture frame molding. My Grandmother Wurtz was so unhappy so far from her friends in St Louis that my grandparents moved back to St Louis where four brothers and a sister followed my father into a family in turmoil. My grandmother was simply unable to take care of the children, and so my father was raised by an aunt who looked after him until his early teens. She was a nurturing guardian, and her carpenter husband generated my father's interest in carpentry. Those interests were passed on to me as a child, and then to my son who now is a carpenter. My Grandfather Wurtz descended into alcoholism, and the family became increasingly

financially stressed. As the children reached an age when they could work, necessity required they do so. My father had just finished sixth grade when he went to work. He loved school but was forced to leave when he had learned reading, writing, and arithmetic. He became one of the most educated people I have met, but that was later, and entirely on his own.

He worked at a variety of jobs in St Louis, few of which I know, but he eventually worked in candy stores, and by the time I was born he was factory superintendent for the Mavrakos Candy Company, a St Louis confectionary landmark. This job rewarded his management ability. He planned the production schedules and supervised a substantial work force, the majority of whom were the women chocolate dippers, those who dipped the variety of centers into chocolate by hand. They liked him and gave him a wallet every Christmas which, since he used only a change purse, provided me a supply I have only recently exhausted. The founder-owner apparently recognized my father's ability to keep things running efficiently, and for someone with little education, the job paid well. The 6 day per week regime, 1 week vacation, and continuing conflicts between owner and workers left him exhausted. He was also an avid socialist who emotionally sided with the poorly paid workers, not the management.

My mother hired him at Mavrakos. She was the bookkeeper for the company, did the initial job interviews, and was clearly one of the super-competent women who ran things as underlings because they were women. My mother was the daughter of first-generation immigrants from Yorkshire and Lancashire, England. My grandfather, Harry Popplewell, emigrated after his farmer and innkeeper father died of tetanus when his hand became caught in a mowing machine. Harry was the youngest son, would inherit nothing, had little future in England, and with his wife and young son, traveled to St Louis, Missouri, at the behest of a relative who lived there. My Grandmother Popplewell was terrified at the sight of her first black man, and both always recalled being startled at seeing their first lightening bugs. My grandfather did what he knew; he became a livestock trader, a rough and tumble expression of free enterprise in growing St Louis in the decade before the 1904 World's Fair. As a child, I was riveted by his tales, but I suspect I missed the best ones when my grandmother, sensing the impending story, invited me to help her with the dishes. Alice, my mother, was born in 1901, was a late last child after her three brothers, and the favorite of my grandmother.

The initial relationship between my mother and father moved beyond work, and they were married by a justice of the peace, and honeymooned by driving to Springfield, Illinois, for a weekend. They had both been frugal, and they used their savings to invest in building a modest house in Webster Groves, a suburb of St Louis. My father deemed it to have the best public school system, and he was determined that I would have the education he did not. My mother thought education was desirable, but she did not bring the passion of my father to that goal. My mother wished she had become a

certified public accountant; my father wished he were a concert violinist or a college professor. I absorbed the business bent of my mother and the intellectual bent of my father, but my father's interests won out.

I was born in 1936, a late child for my father (in his 40s) and my mother (in her 30s), and an only child. My mother stopped work to care for me, which was the proper thing to do at the time, though there is no doubt that she would have preferred to continue working. I was frequently sick as a child with the usual round of childhood diseases, a seemingly continuous round of colds, and scarlet fever. My father continued working long hours, but we usually took trips to state parks on Sundays for picnics and hikes. The high point of the year was the summer vacation trip, which became longer after my father retired, and frequently included his favorite destination, Yellowstone National Park.

I liked school and did consistently well. I was inspired by my fifth and sixth grade teacher, Mary Moore, to read as much as possible, and she would suggest books, particularly on history, which became an enduring interest. I remember Francis Parkman's *The Oregon Trail* as a riveting read. She also had me come in early several times a week to practice my abysmal handwriting, and my mother worked with me on spelling. Their considerable effort failed on both counts. I am convinced poor spelling at least is a built-in characteristic. A high school English teacher summed it up: "Young man, if your livelihood depends on spelling, you will starve," and while I have been saved by the computer, the deficit persists. After a change in my e-mail system, I immediately got returns from friends: "Bob, turn on your spell check."

While I excelled in school work through high school, a nagging disability dating from preschool years was a debilitating stutter. I was given speech therapy both in school and in private sessions with little benefit. Then in junior high school I gave a successful and well-rehearsed talk in the course of running for school president. The debate coach, Dorothy Weirich, suggested that I join the debate team. When I explained that I could not because of the stutter, she simply said that it was irrelevant, and that preparing for debates would help my speech. I agreed to do so with considerable anxiety, and over the high school years my stutter diminished as success in debates increased. Our team won the Missouri state debate championship in my senior year due in part to what I thought was my particularly effective final rebuttal. I had many devoted teachers, but the abilities I use every day result from Mary Moore in grade school and Dorothy Weirich in high school. My parents' determination to provide me a good education shaped my life in ways they could never have imagined.

I adored my father, and the feelings were clearly mutual. His goal was to teach me everything he knew, and he never lost an opportunity to show me how to garden, take pictures, go camping, use carpentry tools, and adopt his attitude that anything can be repaired. He even guided me when I became

obsessed with fishing and assuaged my anxiety over what to do if I catch a fish with an aphorism I have used throughout life: "First we will get the fish on the hook, and then we will worry about getting it off." My father was greatly relieved when my fishing phase ended because he was a vegetarian who felt that there was no need for any animal to die for his lunch. But when I became interested in biology he strongly supported doing research on animals because there was good reason for an animal to die humanely to advance the knowledge from which we all benefit, including animals. He was always hopeful that I might become a scientist though of course regarded it as my decision and never proselytized. Among my aunts and uncles, I was regarded as a bright child, one who someday might even become a dentist.

My only failure in my father's eyes was my limited success in playing the violin. His father had played the violin and taught him to play, and so my father began teaching me before kindergarten, and continued until I had private lessons. I played in the orchestras in grade school and junior and senior high school, but my talent was limited and my desire to practice was negligible. I think my father's disappointment was ameliorated by my success in school and his own diligent practicing after he retired.

I was always shy, and so was not a participant in the social whirl of the suburban high school that was the topic of a TV network program "Sixteen in Webster Groves" filmed some years after I graduated. I was also a clumsy athlete, usually being placed in right field. In high school I accumulated a group of friends who were nerds in today's vernacular. We were all interested in science, were sufficiently quick witted to maintain a lively patter. We had more unbridled discussions on world events than we ever had in the more staid classroom. We all went to college, all became scientists or engineers, and my interaction with them intensified my own interest in science. Our favorite science teacher was Evrard Leek, who taught a course in physics starting with classical mechanics. I can remember to this day the realization that physical phenomena like the force of a pulley system can be described by a simple equation. It was the first insight into what science was about. Essentially, the positive influence of my father as a child had been replaced by an equally positive and dominating one of a peer group.

Oberlin and Deciding What to Do When I Grew up (1954–1958)

I viewed the decision about what kind of college I should go to as a restatement of my father's dictum: Find what you like to do and then spend your life doing it. I viewed college as the opportunity to find that out. So what I wanted was a liberal arts college, but I had little idea of how to even begin to make the choice. One of my high school group was applying to Swarthmore, and he said I should do so as well. I thought it was too far from home; I had never been away from my parents for more than a weekend. He then

suggested Oberlin as being probably as good and only half the distance from St. Louis. So I applied, was accepted, and received a tuition scholarship. It had the advantage of providing a good education, and it had the reputation for actively supporting social causes. This latter point was a significant factor to me because my father's socialism had given me the goal of leaving the world a better place than I had found it. In the fall of 1954, my parents drove me to Oberlin, and I was off to determine what I was going to be.

I began thinking I might major in chemistry, in part because of an inspirational second semester my freshman year taught by J. Arthur Campbell, who emphasized problem solving and not memory—the periodic table was always on the wall. This was my first inkling that I really did not have a great memory, and that I in part compensated by figuring things out, even those things most other students could just memorize. My sophomore year allowed me to look around and exposed me to two exciting areas of science. The first was experimental psychology, which instead of being an eclectic survey was taught from the point of view of the behaviorist, B. F. Skinner. There was no pretense that the Skinnerian view was the only way to understand behavior, but it was taught by George Heise to show how behavior could be quantified and modeled. For me, it was to behavior what the simple equations had been for pulleys. It also included a required laboratory project in which I did a conditioning experiment on rats, which firmly established my interest in animals, their behavior, and what I could learn from the study of controlled behavior. The second was a course on the physiology of the nervous system taught by George Scott, which was skewed toward classic experiments which we repeated in the laboratory on frogs. It was interesting rather than riveting, but again it was the first introduction to the possibility of simple rules: all nerves carried the same impulses, but it was where the nerve started and ended that determined how a nervous system worked. The combination of the two courses opened up a new vista: if it were possible to measure behavior precisely and neuronal activity with equal precision, maybe it would be possible to study how the neuronal activity produced the behavior. While this was a novel thought for me, it was no intellectual breakthrough; the literature on the topic was substantial, as I learned in graduate school.

Among the other hodgepodge of courses I took in my exploration phase at Oberlin was the introductory economics course taught by Kenneth Rouse using Samuelson's now famous textbook. This also demonstrated what could be learned by systematic analysis of a complex system, now an economic system rather than a nervous system. It was riveting, particularly national income economics, but after a follow-up course, I concluded that I liked the opportunity to test predictions of future behavior in the laboratory rather than gathering observations of past behavior. So by well into my junior year I settled on studying the nervous system. For this direction,

there was another decision: medical school or graduate school, which I thought came down to how much I would like treating a single patient as opposed to solving a general problem.

I then had the opportunity to test my research abilities by attending a summer program after my junior year at the Jackson Laboratory in Bar Harbor, Maine, on a stipend provided by the National Institutes of Health (NIH)—the first of what was to become a lifetime of support for my training and research. A division of the Laboratory studied behavior, and I did a study supervised by John Fuller on whether there were differences in motivation for food between genetically obese mice and their normal siblings. I learned a lot about behavior (mice do not press bars like rats) and a bit about motivation in an incredibly profitable summer. I also decided that I probably did not have what it takes to do basic research, and I returned to Oberlin planning to apply to medical schools. I did apply, was accepted by several schools, and decided to go to Harvard. But as my senior year progressed, I increasingly had questions about my decision to abandon research. Would I really be able to remember all the disconnected facts of medical school? Did I really want to spend my life seeing patients? The latter was a realistic concern—I was never gregarious. I later scored off the bottom of the chart for psychology graduate students on a test of social interaction.

The turning point was when a fellow student said I should read Hebb's then recent book, *The Organization of Behavior*. I bought it, read it through, and then reread the parts on "cell assemblies" and "phase sequences." It was the first time I had a glimmer that it might be possible to explain at least simple behavior by understanding circuits of neurons in the brain. I understood that these were hypothetical circuits (but not how hypothetical), but this rekindled my thinking about brain and behavior in specific neuronal terms. Many years later I gave a seminar at Dalhousie University in Nova Scotia, where Hebb was an emeritus professor after retiring from McGill. He came, I met him, and I was able to express my appreciation for his inspiration. I doubt it was a notable event for him, but I was thoroughly rattled by his presence at the seminar.

After rethinking my decision for medical school throughout the fall and winter of my senior year, I decided that I was indeed most interested in experiments on the brain. I also thought that I would be happier in a university than a medical school environment, which for me has generated the ultimate irony: I have spent my entire life in the most rarefied of medical environments, the NIH. So I decided I should go to graduate school, not medical school. Sally Smith, a fellow student at Oberlin who I would marry later that year, was supportive of not only the decision at Oberlin but was immensely helpful and supportive throughout the hardest years of my life, in graduate school and in the postdoctoral years. My Oberlin advisor, however, thought I was "making a grave error." But I think my father's dictum

of “work at what you love to do” had won out. While I have often wondered about the consequences of making the opposite decision, I have never doubted that I made the right one.

Deciding on graduate school in the spring of my senior year generated the obvious problem of getting into graduate school long after application deadlines. My Missouri draft board, which was always desperate to fill its quota because so many in my draft district went to college, also helped to keep my focus on getting into graduate school. The obvious route was to switch to being a graduate student at Harvard, but I did not see much study of the nervous system there. Harvard must have seen what I saw because within a few years Stephen Kuffler arrived and established the neurobiology group. Actually, the basic dilemma for graduate school was that behavior was studied primarily in psychology departments and the activity of the brain was studied in physiology departments. The closest combination of physiology and behavior was in an area referred to as physiological psychology and I opted for that. As in so many times in my life I got by “with a little help from my friends.” Steve Kaplan (who had pointed me toward Hebb) and Rae Kaplan were fellow students at Oberlin who went on to do Psychology at the University of Michigan in Ann Arbor, and they urged me to consider going to Michigan, and in particular pointed out the exciting experiments of James Olds. To make a long story short, I was admitted to Michigan largely through the benevolence of Bill McKeachie, the department chair. Olds took me on, sight unseen, as a research assistant.

Michigan and Jim Olds (1958–1962)

Psychology at Michigan covered the spectrum from learning in rats to clinical psychology. All graduate students took a first year course covering it all. For me such a survey was exceptionally valuable because I had continued my major in chemistry at Oberlin in order to graduate. Entering graduate students also took a set of proficiency tests in 10 areas of psychology. I passed only three: physiological, sensory, and developmental. When I had my first conference with my graduate advisor, he rightly asked why, if I had failed two-thirds of the tests, was I taking biochemistry and physiology rather than added psychology courses. My plan of course was to study not just behavior but brain and behavior and to do so I needed to know much more than what was available in the psychology department. Rather than backing off, I went on to take neurophysiology and neuroanatomy. This was possible because Jim Olds fully supported my logic, and of course I was just trying to construct a program that is now routine in what has become neuroscience.

In fact, I had gone to Ann Arbor in the summer before starting graduate school to start to reduce my course deficiencies in psychology, but the major benefit of the summer was the opportunity to work in the laboratory of Russell DeValois. This allowed me to see single-neuron recording in monkeys

and participate in training monkeys to make color discriminations. I struggled through the summer to train a new world monkey to do a color discrimination, unfortunately one that Russ later showed it could not do. Russ was exceedingly generous, giving his time to someone who knew where the brain was but not much else. The experience sensitized me to the advantage of training monkeys, an advantage I put to use nearly a decade later.

I should say that I almost certainly got the position with Russ because he had graduated from Oberlin. At Oberlin I believe he had been one of the last of Stetson's drivers, students who drove the Chair of Psychology, Raymond Stetson, to and from the department because of an infirmity. One of the earlier drivers was Roger Sperry, who many years later published a paper on mind and brain (Sperry, 1952) and credited Stetson for many of the ideas.

I basically went to Michigan because I was fascinated by the work of James Olds, who became my mentor during graduate school. Jim Olds was famous for his discovery with Peter Milner that electrical brain stimulation could act as a reward in addition to its well-known aversive or arousal effects. Before doing his postdoctoral work, the closest he had come to thinking about the brain was probably his article on "A Neural Model of Sign Gestalt Theory" while he was at Harvard (Olds, 1954). He decided on a change in direction, went to McGill to work in D. O. Hebb's laboratory, and there joined a project with Milner exploring arousal following brain stimulation. Jim told me that he barely knew which end of the rat had the brain and that he learned everything he knew about rat behavior, implanting electrodes, and doing brain stimulation from Milner, whom he described as a brilliant experimenter. He thought that, while the entire experiment was dependent upon the skills of Milner, he did make a major contribution: he noticed that when they stimulated the rat while it was in a particular region of an open field, the rat tended to return to that part of the field. Jim told me this story in about 1958, and I did not have the good fortune to meet Peter Milner until nearly a half century later, in 2007. When I asked about his work with Olds, Milner's description of the discovery was identical to that of Olds, including that Olds did not know one end of the rat from the other, but that it was Olds who made the critical observation in the open field test. I found this a remarkably parallel description by the protagonists, even though the descriptions were separated by nearly half a century. In their classic experiments, they gave the rat a bar to press to produce brain self-stimulation, and the results were immediately recognized as changing the landscape of the brain basis of motivation (Olds and Milner, 1954). The serendipitous discovery of brain self-stimulation catapulted Olds to prominence. I think it also shaped the way he did science.

My approach to science and my fundamental strategy for doing research was subsequently shaped by Jim Olds, and I am forever in his debt. His tragic drowning in 1976 prevented me from ever directly acknowledging my

gratitude to him. I could not have done so earlier because it took me some time after graduate school to appreciate how fortunate I had been to work in his laboratory. And work I did. At that time Jim had a system for running groups of about 20 rats, each in its own Skinner box with a bar to press. One test was for the rewarding effect of stimulation. The rat pressed the bar to electrically stimulate a site in its brain, a counter recorded the number of presses, and in successive periods of about 10 minutes the current was raised, which gave a graph of bar presses versus stimulation current. The second test was for aversive effects of the same stimulation at the same site also at different current levels. Now the current was pulsed through the electrode at regular intervals and the rat could press the bar to escape the stimulation; the higher the rate of bar pressing, the greater the presumed aversive effect of the stimulation. Some sites produced self-stimulation, some escape, and some both, which Jim called ambivalent sites. There were some four or five groups run every weekday, and mine was the late afternoon run. I did this throughout my first year of graduate school, from September 1958 until the following summer. The work was tedious but tolerable, and it showed me how to do serious investigation of behavior: build a machine to produce data in adequate amounts to draw substantial conclusions.

I did not get off to a great start with Jim. As I was starting in his laboratory, he gave me a précis of what the experiments I was running were about, and he gave me his reprints to read. I wanted to make sure I was not missing anything (the days before Pub Med!) and I asked him, is that all? He cocked his head as he was wont to do when slightly irritated or amused, and said, "I have just given you my life's work, and you ask me, is that all?" A month or so later I raised my arms to put on my lab coat, hit the bar going across the room from which the stimulating leads went down to each rat, and knocked the whole 20 foot bar to the floor. This would have been easily fixed were it not for the 20 little pools of mercury that acted to minimize twisted leads when the rats rotated in their boxes. So there was a mercury spill that required cleanup and repainting. I shuddered to think what Jim would do after the debacle, but he said nothing, presumably realizing my mortification and knowing that it was not the first time it had happened.

Jim Olds was direct and forceful, that is to say blunt, and as an insecure graduate student this was intimidating. Few graduate students continued working with him, and I was the first to do so from start to finish. A watershed for me occurred in the second year when for an experiment on cats we needed to take a sick cat with an implant to a veterinarian. At that time, the only way to have an animal treated was to take it to a small animal veterinarian, but I was loath to take a cat with a cranial implant into a waiting room. So we took another unimplanted cat with the same symptoms and asked for medication for both of them. Jim got word that I had paid to have a normal cat medicated, and he berated me for taking any cat that had just

sneezed to the vet. At a pause, I explained my logic, and he cocked his head, and said, "That was perspicacious of you." When I looked up the word, I realized it was a compliment. I had an easier time with Jim after that.

When I arrived at Michigan, Jim had told me that undergraduate rules for success no longer applied; as a graduate student grades were irrelevant, discovery was all: "Do what needs to be done to satisfy academic requirements, but direct your energy to research." I took him seriously, and inadvertently tested his resolve. I took his course on motivation, got a C+ (comparable to an unthinkable D- at Oberlin), but he never said a word. When I had enough credits for a Masters degree, I took the form for Jim's signature, but he refused to sign it. If he did, he said I might think I had accomplished something, which I had not. These were good examples of the guidance I got from Jim, forceful and almost always correct. Finally, he would not permit any time to be taken from research for teaching—it was just a distraction from thinking about your research. He only relented after I had finished writing my thesis in my fourth year. I jointly taught an undergraduate psychology course, and, while I thoroughly enjoyed doing it, Jim was right on the time it took.

I came to realize that Olds regarded my first year of monotonous measurement of self-stimulation as both training and a test of my ability to stick with a project. I seemed to have passed the test, because toward the end of that first year he suggested a project that I would do largely on my own. The goal was to explore an aspect of self-stimulation that he thought was promising: whether the motivationally relevant cluster of nuclei in the amygdala produced rewarding or aversive responses in rats. I already knew how to do everything from electrode implanting to behavioral testing, so the project progressed rapidly, and I was able to show that stimulation of the corticomedial division of the amygdala produced more reward behavior and the basolateral division produced more aversive behavior.

By my second year of graduate work, Jim Olds had shifted his interests from mapping the motivational effects of brain stimulation to exploring how brain stimulation might provide the reinforcement for learning. He was looking for changes in activity during learning in single neurons in the brain. My contribution was to make the microelectrodes, and I was able to make stainless steel electrodes using insect pins and tungsten electrodes using the Hubel method (Hubel, 1957). They were probably not great, but they did record some cells some of the time. I then recorded cells in a number of projects after my amygdala experiments, including looking for changes in neurons before and after learning and asking whether there were changes in the brain related to visual attention. None of these projects produced any useful results, but they introduced me to learning and attention and emphasized to me the value of exploring where the results were uncertain. I had imprinted on Olds own exploratory method.

In the middle of my third year, Olds suggested that I use the self-stimulation study of the amygdala that I had done in my second year as the central part of my Ph.D. thesis. I coupled this with a largely unsuccessful attempt to establish a neuronal basis for self-stimulation by trying to see differences in neuronal activity in the amygdala locations where stimulation was rewarding as opposed to aversive. I gave my first scientific talk on the amygdala at the spring meeting of the American Physiological Society on a 1-day trip to and from Atlantic City. It was a talk on the afternoon of the last day of the meeting and there was even a question. When I sat down, the person next to me said, "That was an excellent talk" (due to Olds demanding coaching) and asked, "Do you know who asked the question?" I had not a clue. He said it was Alexander Forbes, a Professor at Harvard, a leading physiologist, and clearly one of the most considerate scientists of all time.

The trip was rushed and tense because our first child was due, but William Robert did not arrive until several weeks later. He was the most active boy imaginable and was into everything as soon as he could crawl. The only advantage of our tiny apartment was that we did not have much for him to get into.

I finished my thesis and submitted it in 1962. Jim did not approve of my prosaic title, "Self-Stimulation and Escape in Response to Stimulation of the Rat Amygdala," but I thought it should convey exactly what the study was on, and his view was that it was my thesis. My memory is that the editor of the Michigan Daily, Tom Hayden, the California activist to be, was also taken by my title. He wrote an editorial related to mindless science and used my title as his inspiration. The title of our published paper became "Amygdaloid Stimulation and Operant Reinforcement in the Rat" (Wurtz and Olds, 1963).

As I neared the end of my time as a graduate student I was obviously thinking about what research direction to take. Vernon Mountcastle had given a seminar on his elegant recording in the somatosensory system, and I left thinking that he was listening to what neurons were saying while I was electrocuting them. Continuing brain stimulation did not seem very promising, and it turned out that real progress did not come in this area until the ability to manipulate transmitters and their receptors became possible much later. But the major advance for me came in a summer I spent at Woods Hole in 1961 as a Grass fellow. I had applied with the strong support of Olds and a project that proposed to study the brain of the squid during a conditioning task. This was to be done in my 2 months stay, which must have given the review committee a laugh, but it also fit with the Grass-sponsored Alexander Forbes lecture given by J. Z. Young, the world's expert on the squid brain. My experiment did not work. I managed to record from the awake but restrained squid, but only from the optic nerve. The salient event of the summer, however, was a talk by David Hubel at one of the regular

Friday evening lectures. I had been unaware of the work and found it mesmerizing. David stayed several days after the lecture, and I was able to talk with him. He also invited me to stop by his laboratory at Harvard on my way back to Michigan in order to sit in on an experiment in which he and Torsten Wiesel were mapping the orientation specificity of V1 neurons using long penetrations. He even put us up overnight and invited us to dinner. To say that it was a life-changing visit would be an understatement. Unfortunately, during the dinner break the cat died, and it was only much later that I realized that they paused for dinner at home only occasionally. I thought for years that by associative learning I must be linked in the minds of Hubel and Wiesel to a dead cat.

Had there been a possibility of doing a postdoctoral fellowship with Hubel and Wiesel, my research direction would have been set. But that turned out not to be possible, and this let other issues command my attention. It is difficult now to appreciate the intensity of feelings about the threat of nuclear war that prevailed then. I had rung door bells in Ann Arbor for Kennedy, had listened to his inaugural speech (by taking the ground wire off the recording amplifier used to record neurons from the rat brain), but was dismayed at his failure to do anything other than increase the nuclear arms race. It all led to the inevitable question, Why would I be working on the brain if the world was about to be blown up in a nuclear war? So I decided to split my time for the next 2 years between being on the staff of the Committee for Nuclear Information in St Louis and a research fellow at Washington University. I expected Jim Olds to be disappointed with my direction, and he was. He was also remarkably supportive of my effort, but said he hoped I would return to science. His parting comment was that he thought I could become a department chair. When he saw my crestfallen look, he quickly added that he meant it as a compliment.

St Louis and Banning the Bomb (1962–1965)

The philosophy of the Committee for Nuclear Information, which consisted of scientists and physicians in St Louis, was that the issue of nuclear weapons was a political not a scientific one, but that intelligent political decisions depended on an understanding of the underlying science. It was the public that needed this understanding because that was the ultimate source of decisions in a democracy. In hindsight, this sounds a bit utopian, but in fact changes in political direction frequently do result from a welling up of public support or disapproval, as in the case of the Vietnam War. My role was as a scientist, contributing half my time to research and to articles that appeared in their publication that had a small circulation, but whose influence was magnified because its articles were frequently picked up by newspapers. A major leader was Barry Commoner, who had a keen eye for putting information out in ways that would attract attention. I also benefited from his

ability to dismember my articles, particularly one on the effects of nuclear weapons (Wurtz, 1963). The decision to move testing underground, rather than ending it, was a brilliant political maneuver by the Kennedy administration. For the world it was a disaster because the nuclear arms race continued unabated, but the public interest in the nuclear threat largely vanished. For the Committee this led to discussions of what to do next. The key point that emerged was the recognition that nuclear fallout was only one environmental hazard, and that the real issue was the environment itself. In an exceptionally foresighted move, the group gave their publication a new name: Environment.

I felt that I had not accomplished much in the time I had spent with the Committee, nor had I done any serious research. At this point I realized that attempting to go in two major directions at the same time (ending nuclear war and understanding the brain) was beyond my capacity. Considerably disillusioned, I went back to brain research.

I was cheered, however, by the birth of our second child, Erica. She was not only a beautiful and happy child, but routinely demonstrated the phases of sleep that I was studying in one of my lab experiments. One night in particular, I was caring for her while Emilio Bizzi and I were discussing rapid eye movement sleep. Erica demonstrated the transition directly from wakefulness to rapid eye movement sleep that babies do readily, avoiding the slow wave sleep of adulthood. With William and now Erica I resolved to at least take Sunday off and went for picnics and hikes to many of the places near St Louis that I had gone to as a child with my father and mother. Bill and Erica liked the trips; their favorite was to the zoo.

My research fellowship at Washington University was in the Physiology Department, but my intellectual mentoring was in the Neurology and Neurosurgery Laboratories where interest in the brain was then centered. I continued on lines I had begun in Olds' laboratory, starting with an attempt to see whether slow potentials in the brain, thought at least locally to reflect dendritic activity, changed during learning. But James O'Leary, chair of the Neurology Department, wisely thought anyone who studied slow potentials ought to know about their origins. Because it had recently been shown that the potentials varied with the phases of sleep, he suggested that I start by studying sleep, and my direct mentor Sidney Goldring concurred. So I adapted the laboratory's DC electrodes to record from cats during sleep as a route to understanding the potentials (Wurtz, 1966). The more I learned, the clearer it became that I had no idea what the origin of the slow potentials was. The message I took from this series of experiments was that while recording brain electrical activity during an animal's behavior was a frontier of neurophysiology, it was only a frontier if one knew what the source of the activity was in the brain.

I therefore switched to another project related to learning where I knew what I was recording, in this case in the marine mollusk, *Aplysia californica*.

The experiment was to test Hebb's hypothesis that a synapse was strengthened when the excitatory postsynaptic potential (EPSP) was followed by an action potential in the postsynaptic neuron, and weakened when it was not. Two factors made the test possible. A graduate student, Vincent Castellucci, was recording from *Aplysia*, and I was impressed with his skill and the ease with which the intracellular recording showed the EPSPs. The second factor was that Sid Goldring had participated in the LINC evaluation program, a program based at MIT to introduce computers into the laboratory, and the program had provided a computer which he had brought with him. I learned what it could do and how to program it (in assembly language). I realized that I could use the LINC "on line" to recognize a particular EPSP shape and have the computer within milliseconds pass current through the postsynaptic neuron to produce an action potential. Over time that EPSP should then come to more effectively drive the neuron. Vincent was a wonderful collaborator and, together with a summer student, we programmed the computer and did the experiment (Wurtz et al., 1967). It did not work; we found no effect of the contingent depolarization of the postsynaptic neuron. With the benefit of subsequent knowledge, I realized that a key factor might have been that I was depolarizing the cell body but in this invertebrate the synapses were down on the axon. To this day I regard this as one of my cleverest experiments, but of course a failed one.

I also realized that my understanding of neuronal physiology was very limited and, if I were to study neurons in the brain, I ought to know more about them. Many of my discussions in St Louis had been with Emilio Bizzi who had moved to Ed Evarts's laboratory at the NIH. He urged me to come to the NIH and, after I visited him there, I could see his point. Largely through the good offices of O'Leary, Goldring, and Bill Landau in St Louis, Karl Frank at NIH agreed to let me come to use space that was available for a year. I was reluctant to leave such a supportive group in St Louis, but for a year it would be worth it. Just before I left I had the opportunity to give a talk at The Needlework Society, run that year by Bill Landow who gave my talk on slow potentials during sleep the title "Shifts That Pass in the Night." My departure for the NIH was delayed by the terminal illness of my father, and I did not leave for the NIH until October 1965.

Developing Visual System Recording in Awake Monkeys at the NIH (1965–1969)

At the NIH I joined the Laboratory of Neurophysiology, which was jointly run by the National Institute of Mental Health (NIMH) and the National Institute of Neurological Diseases and Blindness (NINDB) with Wade Marshall of NIMH as chief of the Laboratory and Karl Frank of NINDB as chief of the Spinal Cord Section within the Laboratory. I quickly learned that names did not mean much, and that there was little relevance of which

Institute you worked in. In the Spinal Cord Section, Karl was studying *Aplysia*; Phil Nelson, Norm Robbins, and Gerry Fischbach were studying development; and Bob Burke was actually studying the spinal cord. I continued recording from *Aplysia* and did reach my goal of understanding more about neuronal function, which of course then led to the question of whether to continue these experiments. I talked to and visited a young psychiatry resident at Harvard, Eric Kandel, whom I was convinced was actually succeeding in studying learning in *Aplysia* and, had I continued in that direction, there is no doubt I would have gone to Eric's laboratory. But I realized that I missed studying the rich behavior of higher animals, including measurable cognitive behavior, and I began thinking more about returning to the study of neuronal systems in the brain of mammals.

I was increasingly drawn to the primate because of the ability to control its behavior through training and because much of behavior was so similar to that of humans. This interest was heightened by my contacts with Edward Evarts at the NIH who was studying limb movement in awake monkeys. I also returned to thinking about Hubel and Wiesel's work and the insights into the organization of neurons that they had produced. Specifically, I thought that if I could do the Hubel and Wiesel experiments in awake monkeys, I might see activity beyond the visual responses in cortex, including correlates of such cognitive functions as perception and attention. As if all this would be in V1!

The obvious place to do this was Ed's laboratory, but Ed had no position open. There was, however, a position in Ichiji Tasaki's Laboratory of Neurobiology in NIMH. Tasaki was famous for discovering saltatory conduction of nerve impulses along myelinated nerves. He was then concentrating on nerve conduction in squid, including experiments that did not agree with Hodgkin and Huxley's conclusions, which largely isolated him from the larger NIH community. He had also recorded from the brains of cats (I believe he was the first to have recorded single neurons in the lateral geniculate nucleus; Tasaki et al. 1954), and he headed a Laboratory that was intended for the study of the nervous system at many levels. I applied for the position and again almost certainly got it on the basis of the recommendations from St Louis because Tasaki knew my St Louis mentors well, having spent several years there shortly after the end of World War II. I explained to him what I wanted to do: study vision in awake monkeys. He did not wince or even blink, and summed up our conversation by saying, "I learn from Professor Squid, you learn from Professor Monkey". Over the decade I was in his laboratory, I came to realize how outstanding a scientist Tasaki was both at the bench and in his innovative thinking. He was happy to have me, in part because I was off struggling with my Professor while he communed with his. I began in Tasaki's laboratory on July 1, 1966. Instead of returning to St Louis in a year, I have stayed at the NIH for over 45 years.

The problem with studying the visual system in the awake monkey was the rapid or saccadic eye movements that moved the retina several times per second. These saccades are integral to our remarkable vision; our one high-resolution region in the fovea is directed to successive regions of interest by the saccades. Each time the eye moves, however, a stimulus falling on the receptive field (RF) of a neuron, as in Hubel and Wiesel's experiments in anesthetized cats, would be displaced to a different part of the retina. If I were to study the visual system while it was actually being used for vision, I would have to solve this problem. The solution was obvious: study the RF of a given neuron while the monkey fixated for several seconds in order to obtain a reward, then let the monkey make saccades for a few seconds and then require it to fixate again. Instead of a continuous period for the analysis of the RF in the anesthetized animal, I would have a series of two to three-second time windows in which to study the RF. I had gone up to Hopkins to visit David Robinson's laboratory and seen that Albert Fuchs had trained the monkeys to make saccades and pursuit eye movement to obtain a reward (Fuchs, 1967). Why should training the monkey not to move its eyes be any harder?

I got the answer to that quickly enough; monkeys liked to fixate but on what they chose, not what I chose. One look at what I wanted them to look at, and they were done. I was clearly going to have to reward them just for fixating. Here I followed one of the lessons from Olds' laboratory: if you need to shape behavior by repetitive trials, build a machine to do it. I built a circuit out of a type of logic cards that I had used at Washington University. Each of these DigiBit cards had a logic element, such as an And gate, Or gate, or Flipflop, or a switch for an input or a relay for an output. It required knowing some tricks to get the circuit to work, but the circuit was in principle logical and therefore simple to diagram. I built a circuit that turned on a slit of light on a screen in front of the monkey when the monkey pressed a bar, and after a variable length of time, changed the slit orientation. If the monkey indicated it saw the change by releasing the bar, it received a fruit juice reward. For the stimulus I found a small indicator light that was designed for soft drink machines which had nine bulbs that projected through one of nine lenses onto the back of a small plastic screen. Changes of slit orientation were made by turning off one bulb and turning on another. It was a simple and rugged device that we continued using in the training setups for many years.

The goal of the training was to make the change in the stimulus so small that the monkey would have to direct its fovea toward it in order to detect the change. The training started out with large slits and large orientation changes, progressed to smaller slits and smaller changes, and ended with a small spot that just dimmed. The first monkey learned the task with amazing ease. Ethel was, however, a high-strung monkey and had the habit of biting her nails (a trait I have never seen again). By the ease of her training,

I concluded she was an ideal monkey for the more complex tasks I expected to move on to promptly. I then began training another monkey and thinking about recording.

My laboratory room was in NIH Building 9, which housed all of the behavioral-based monkey experiments, and was one of the early NIH buildings. It was well worn and was scheduled for demolition. Forty-five years later it is still in use, but it is inadequate for housing monkeys and can only be used for humans. Another resident of Building 9 was Ed Evarts, who had just worked out the techniques for restraining the monkey's head and implanting recording cylinders in the skull (Evarts, 1966; Evarts, 1968a; Evarts, 1968b). Ed had also modified a microdrive developed by David Hubel for advancing the microelectrode in the brain of awake cats (Hubel, 1959). The NIH had a central machine shop with superb machinists where Ed had all his parts made; Ed simply made me a list of what parts I would need and said to give the shop the list. I did just that, and I had what I needed within a few weeks. Setting up for recording was a dream, and Evarts always went out of his way to answer any question and address any problems. I also had had the generous help in learning how to handle the monkey from Hal Rosvold, who was Chief of the Section on Neuropsychology. He and Mort Mishkin, to whom I directed many a naïve question, were in the same building. It is difficult to imagine a more ideal environment for what I was trying to do.

I had learned to do the actual recording from awake monkeys by sitting in on experiments with Emilio Bizzi, who was then finishing up his experiments on the frontal eye field before moving to MIT. His recording room was in the dismal basement of Building 9, as was my office, and both were reached by an elevator whose every move seemed likely to be its last. I had already watched an experiment in my earlier brief visit to Hubel and Wiesel's laboratory, so I knew what I needed the monkey to do. I also watched the surgical preparations and procedures of Mort and the specific implant procedures of Ed. So in November 1966, I did my first implant on the second trained monkey, putting on an Evarts' head holder, and a recording chamber placed just anterior to the occipital bony crest.

During the training procedures I had to rely on the monkey's performance to evaluate whether it fixated. With the monkey's head now restrained for recording, I could at last measure the eye movements to see that it was actually fixating. Over the summer I had worked out an eye movement recording system based on the well-established electrooculogram that measures a DC potential across the eye; as the eye turns, the amplitude of the recorded potential changes. I pasted electrodes onto the monkey's shaved skin near the eyes and, of course, this had to be done before each session. It was immediately clear that the monkey was fixating for the several seconds that I thought it was. It was equally clear that I could not measure the small drifts and microsaccades during fixation, so I would not know anything

about such small movements. In order to minimize the effect of any residual eye movements, I resolved to study RFs that were at least 5° from the fovea.

I thus had the following: a monkey trained to fixate; a recording chamber over what I hoped was V1 cortex (then referred to as striate cortex); a microdrive moving a glass coated platinum electrode (Wolbarsht et al., 1960) that Ed had found would penetrate the dura; the EOG system that I hoped would record eye movements; a projector with a solenoid operated shutter that would project a stimulus on the RF just for the time that the monkey was fixating; all sequenced by DigiBits. While I had not done any of the specific tasks required by this experiment, I had had some experience in doing all the components such as making microelectrodes, training animals, and recording from neurons (Michigan), and recording DC potentials and DigiBit programming (St Louis). But here everything had to work at once, and nothing could be tested until the monkey's head was restrained and that required that first surgery. Learning to get the eye electrodes pasted on so they stayed on, getting the microelectrodes through the dura, isolating spikes, and then getting the monkey to do the fixation task, all at the same time was the challenge I had not adequately anticipated. Over several intense weeks, this all worked well enough so that I could finally try to find the RF of an isolated V1 neuron.

My first goal of course was to see if the fixation in the awake monkey was good enough to verify that V1 neurons responded preferentially to oriented slits of light rather than just to spots of light. On the day before Thanksgiving, 1966, everything worked at the same time for the first time. I had a well-isolated neuron that responded much better to slits than to spots and best to a slit oriented slightly off the vertical. I was very thankful that Thanksgiving.

I was able to verify the orientation selectivity in the next week, but by that time the dura over the brain was sufficiently tough that I could not get electrodes through it and the recording on that side of the brain was over. I was incredibly relieved that the fixation was good enough to record neurons that showed orientation selectivity. I had essentially done the Hubel and Wiesel experiment just as I had seen them do it, but in the awake monkey. On the other hand, I had done nothing else. Because the method did work, I then needed to work on presenting different stimuli, collecting and storing the data, and making sense of it. Here my previous experience provided me with little support, and I spent most of the next year catching up on presenting the stimulus and looking at the neuronal activity. For the stimulus I had initially used a series of slides with several slit sizes and with eight orientations for each size accessible in a Carousel projector. I managed to replace this with a series of slits that I could rotate using a dove prism, and eventually with a slit diaphragm that produced a slit of any size that I rotated by hand on successive trials. This was all mounted on a drill press

stand that allowed me to direct the slit toward the part of the field where I had located the RF with a handheld flashlight.

Displaying and saving the neuronal responses was more of a challenge. I first needed some way to convert the spikes into a pulse that could more readily be displayed and eventually stored. For this I copied the "raster" that Ed had built (Wall, 1959). A Schmidt trigger first converted spikes greater than a given amplitude into a voltage pulse, and then these pulses were displayed as dots on the sweep of the oscilloscope by intensifying the beam at the time of each spike. Ed's device also had multiple discrimination channels so that up to three spikes could be separated. Ed laughed when he saw that I had duplicated the channels because in the years he had used it he had recorded two discriminable neurons only occasionally, and he thought if he recorded three at once it would be declared a national holiday. Storage of the data was on a Polaroid print of the raster on the storage oscilloscope screen or of individual spikes on a sweep triggered by the DigiBits. Many other problems had to be solved, but with a little flexibility in stimulus presentation and some data storage, I could proceed with experiments.

What I found was exciting in one respect, but disappointing in another. First and foremost I was able to identify neurons that responded best to oriented slits and to verify their distinction between simple cells and complex cells. I also found many neurons responding to spots as well as to slits (nonoriented cells) that were not seen in cats but were in monkeys (Hubel and Wiesel, 1968). I also found neurons responding to motion better in one direction than the opposite direction as found in the cat (Pettigrew et al., 1968). I was at the same time working on the visual response to stimuli during saccades, so the first publication on visual responses of V1 neurons was not published until 1969 (Wurtz, 1969c). On the one hand, I was disappointed that I did not see something new for my efforts, which I think was in part due to the qualitative analysis I did and in part due to my wild expectations of what V1 cortex might be doing. I would not, however, have expended all my effort just to show that Hubel and Wiesel were wrong because I was counting on their observations as the springboard for a leap into understanding the neuronal basis of cognitive function.

At this point, I did not get a lot of reinforcement from the field. This is understandable because I had not discovered anything new, just that what Hubel and Wiesel had so elegantly demonstrated was readily observed in the awake monkey. I was encouraged when Torsten Wiesel made a brief stop at my laboratory, and when Gerald Westheimer viewed the verification of Hubel and Wiesel's results in an awake animal as an essential advance in studying the visual system. Ed Evarts had been cautious about the outcome of the experiments because he worried that the quality of fixation of the trained monkeys might not be adequate to keep the stimulus on the RF, but he was impressed by the consistent visual responses to the same stimulus over a series of fixations. I also thought that, if a technique was worth the

bother, the results obtained by using it would prove the point. So I did not think I needed any methods paper beyond the methods section of the V1 paper in 1969. This was a mistake that probably slowed adoption of the technique.

The Superior Colliculus (1969–1972)

After determining the RFs of V1 neurons, the next experiments I had in mind were the obvious ones related to how the visual system dealt with the incessant movements of the eyes. The particular question I thought was “low hanging fruit” was how the visual system reduced the blur of the visual field swept across the retina with each saccade, a process referred to as saccadic suppression. A controversy in the early 20th century was whether there was a “central anesthesia” that blocked out vision during the saccade (Holt, 1903) or whether there was simply a reduction in sensitivity (Dodge, 1905). Now I had the opportunity to address this question directly because I could record neuronal responses at the first cortical neurons in the visual pathway. Did they respond, or was there a central anesthesia that turned them off? They responded. In addition, by comparing how the V1 neurons responded as the eye swept over the visual field to how they responded to comparable visual motion when the eye was stationary, I could show a qualitative similarity that clearly ruled out central anaesthesia (Wurtz, 1969a; 1969b; Wurtz, 1968). I had the satisfaction of having discovered a little something at last.

If I did not see the active suppression in V1 perhaps I would see it in the other branch of the visual pathway that went not to cerebral cortex but to the roof of the midbrain, the superior colliculus (SC). So in early 1969, I made some recordings in the brainstem that I hoped were in the superior colliculus, did histology, and found that I was indeed occasionally in the SC. I then shifted recording to the SC, but there was a big difference between SC and V1. Here I had no previous recording to simply verify. I thought I could get a general idea of the activity in the structure and then proceed with my planned experiments, which turned out to be exceptionally naïve. The next 3 years were going to be spent beginning to figure out the structure and function of the SC, not its relation to saccadic suppression. This was to be the first of many shifts in my experimental direction in which I started looking for one particular brain mechanism but would end up studying quite a different one.

My trepidation at the task was ameliorated by Michael Goldberg descending onto the scene in the guise of my first postdoctoral fellow. I say guise because within a year he had become a full collaborator. Mickey as a medical student at Harvard had spent a summer in Hubel and Wiesel’s laboratory. There he heard Peter Sterling’s favorable comments on my work after hearing my maiden talk at the fall American Physiological Society

meetings (Wurtz, 1967). Mickey was specifically interested in the NIH post-doctoral matching program because of the doctor's draft which funneled young doctors to the raging war in Vietnam. Happily, Ed Evarts did not have a position available, but Tasaki had provided me with one, so I did. The match was made, and Mickey showed up on July 1, 1969. His coming was in my view the only known benefit of the Vietnam War.

But in spite of my amazing good luck in having Mickey come to the lab, the SC was still recalcitrant. We found neurons with visual responses as expected but also discovered neurons that discharged before saccades. To our dismay we also found a host of other neurons with many characteristics that we later realized were from the deepest layers of the SC. Before realizing that, the results were so confusing that after a particularly trying day, Mickey opined that he now understood why there was an SC in the brain: one example of every type of neuron in the brain had been placed there to provide practice for neurophysiologists.

With the aid of marks made by passing current through the microelectrode, we gradually came to recognize that neurons with only visual responses were in the superficial layers, and those with saccade-related activity were in the intermediate layers. We then concentrated on these neurons. Each time we obtained histology, however, we had to euthanize a trained monkey, so the problem of localizing where we were recording was a costly one, but it did give us a chance to look at the results we had while training the next monkey. Not all marks could be found, and correlation with recorded neurons was often ambiguous. The ultimate setback was at last having an absolutely certain mark on a nicely stained section perfect for an illustration but with a fatal problem: it had a fold in the mounted and stained section. This we remedied by placing a strip label over the fold that identified the SC layers (Fig. 1 in Wurtz and Goldberg, 1972a).

The tasks we used to explore the relation of the neurons to behavior became increasingly varied, and each time we changed the task, we had to change switches on the DigiBit control panel. For more complicated tasks, we had to change the wiring on the back panel. Figure 16.1 shows us with the recording equipment and the inset shows the back of the DigiBit panel. We resolved to switch to a computer, but not until finishing the ongoing set of experiments. We realized that we could study the brain or the computer, but not both. We worked diligently for over 2 years trying to put the SC pieces together. I remember recording one night when the whole laboratory building was totally abandoned except for us. It was the night of the moon landing. We decided to forgo watching TV because we were having particularly good luck recording; inner space won out over outer space.

Results of our experiments were published in four papers in 1972 after a note on saccade-related neurons in *Science* early in 1971 (Wurtz and Goldberg, 1971). The first of the four was on neurons with visual responses

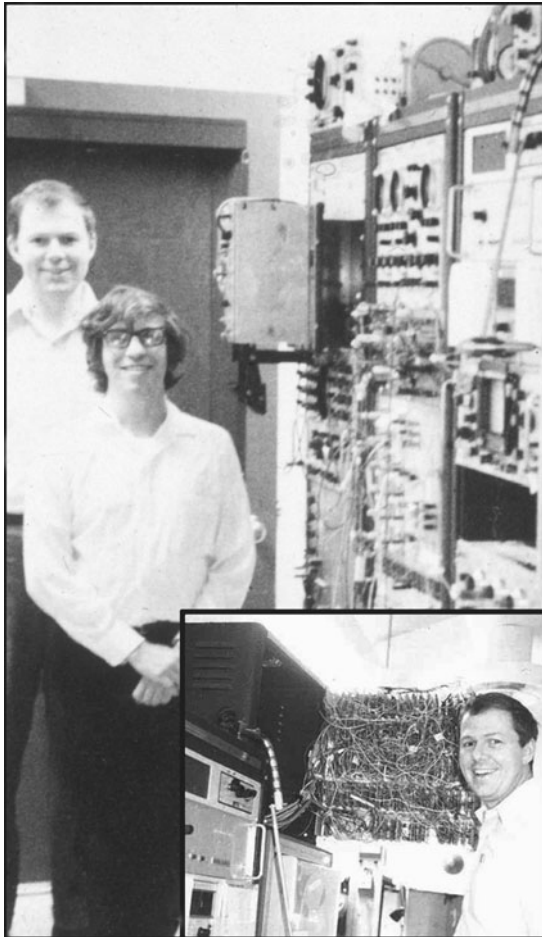


Fig. 16.1 Bob Wurtz and Mickey Goldberg in 1971 with the electronics used for recording from the superior colliculus. The inset shows the wiring of the DigiBits used to control the monkey's behavior. The white tags indicate which wires had to be moved each time the behavioral task was changed and the correct pin location for that wire on each task.

(Goldberg and Wurtz, 1972a), which established that the SC required only spots of light rather than oriented slits, had large RFs compared to V1, and had little directional selectivity. The latter point differed from the finding of directionally selective motion neurons in the cat (Sterling and Wickelgren, 1969), and we labored over several monkeys to make sure our failure to find them was not our error. They are not there, and it was not until later that

directionality in the interaction of center and surround in SC was recognized (Davidson and Bender, 1991). We did see some suppression related to saccades, but this original purpose in studying the SC was lost in the excitement over all the other unexpected observations.

The second paper was on enhanced visual responses related to shifts of attention (Goldberg and Wurtz, 1972b; Wurtz and Goldberg, 1972c), or more exactly our inference that the monkey attended to a stimulus before it made a saccade to the stimulus. We noticed this enhanced response by just listening to the visual response on the loud speaker; the response seemed stronger when the monkey made a saccade to the stimulus than when it did not. We devised a simple task in which we looked at the response to a spot of light in its RF while the monkey fixated and when it made a saccade to the same spot of light. The key criterion of an attention experiment was met because it was the same stimulus in both parts of the task, but the enhanced response only occurred when the monkey shifted its attention to the stimulus to use it as the target of the impending saccade. The enhanced response was not just a general arousal response because it did not occur with saccades to other regions of the visual field. To our knowledge this was the first potential single neuron correlate of attention found in the primate brain. It also was cited as one of the key observations underlying the development of the motor theory of attention by Rizzolatti and his collaborators (1983).

The third paper described the saccade-related neurons that became active before saccades to limited regions of the visual field (Wurtz and Goldberg, 1972a; 1971). We coined the term "movement field" for this region of the visual field as a parallel term to receptive field. The saccade-related activity was before the saccade and we struggled to avoid referring to it as a response to the saccade, a problem the current term "response field" for both visual and saccade activity ignores. We showed the size of the movement fields, that they were centered like the visual activity in the contralateral visual field, and that activity was related to saccades and the fast phase of nystagmus. The fourth paper tested the contribution this circuitry made to the generation of saccades by making electrolytic lesions in the SC and then testing the monkey's ability to make saccades to the region of the visual field related to the lesion (Wurtz and Goldberg, 1972b). The result was astonishing. After seeing all this machinery from visual responses, to a shift of attention, to saccade-related activity, we expected the monkeys to be devastated by the SC lesion. They were not. Within a day when we tested them they could readily make saccades to the affected visual field, and they became better and more accurate over the following days, showing that whatever it did, the SC was not essential for the generation of saccades. What did not recover was the latency of the saccade; it was always lengthened no matter how long we studied the monkey after the SC lesion.

Use of the awake monkey in the SC experiments allowed us to show the transition from sensory processing to the generation of movement in the

same structure, and to gather numerous clues on other modulations. But we missed working out the map for visual and movement processing (Robinson, 1972) because we did not use electrical stimulation as others did (Stryker and Schiller, 1975). We did, however, identify activity that we deemed was related to a cognitive function: visual attention. We therefore regarded the SC as playing a more global role than just the generation of saccades. This was in contrast to the view of the Schiller laboratory that the SC was more specifically related to saccade generation. These differing views were summarized in two articles in the same symposium in 1972 (Schiller, 1972; Wurtz and Goldberg, 1972d), but the resolution is clear: it probably contributes to both. In addition it is not an entity unto itself, but rather one step in a pathway descending from cerebral cortex and, as we found later, a step in a pathway ascending to cortex as well.

Refining Recording in the Visual System of Awake Monkeys

After recording in visual cortex and superior colliculus, it was clear that the visual system and its relation to perception and to eye movement could be studied in awake monkeys. The problem was that the barriers to doing so were substantial. It is worth a digression to emphasize the developments that have made recording in the visual system of awake monkeys more generally accessible.

The method of restraining the head and recording single neurons in monkeys was worked out by Evarts and, while there have been many changes, his fundamental methods are in use today. Recording eye movements was more of a problem. The best method was the magnetic search coil technique of David Robinson and Albert Fuchs (Fuchs and Robinson, 1966; Robinson, 1963) that gave remarkably low noise eye position information using a coil of wire surgically placed under the eye muscles. The drawback was that placement of the wires under the muscles could produce strabismus in the implanted eye. Since I was trying to study the normal functioning of the visual system, I was reluctant to incorporate a technique that could produce double vision. I therefore used the EOG method because it could produce no harm. But it was an awful system with noisy signals that were acceptable for recording the change of eye position saccades but had too much drift to register eye position. In planning experiments with Stuart Judge to see what would happen to V1 neurons when the visual image was stabilized, it became essential to measure the eye position exactly in order to produce the stabilization. After trying a number of approaches, including a contact lens carrying the eye coil as was done in humans and scleral reflection as was also used in humans, the best solution seemed to be a slight modification of the Robinson/Fuchs technique. Instead of threading the wire under the eye muscles and running the possibility of damage to the muscles, the new approach simply placed a preformed eye coil in front of the muscles

but still under the conjunctiva. The report of the technique by Judge, Richmond, and Chu (1980a) is probably one of the most cited papers from our laboratory. It was a minor change, as was Robinson's use of multistrand wire in the coil (so that one wire breaking would not end the usefulness of the coil), but the improved eye movement recording was a critical step in making the study of the visual system in the awake monkey a standard technique.

The ability to know where the eye was directed also made it possible to take another major step: training the monkey on more complex tasks to study cognitive behavior. With my original technique, I rewarded the monkey just for fixating, and I lost the opportunity to train the monkey on most cognitive tasks. Once eye position could be measured, the monkey's fixation could be controlled by requiring the monkey to keep the eye within a given distance of the target in order for it to proceed to a more complex task for which the reward was now given. The awake monkey could now be used for the variety of tasks, including the complex discriminations and decisions that are now used in laboratories throughout the world.

More complex tasks required better control of the multiple events in the experiments: continuous recording of behavioral responses, eye position, neuronal activity, and modifications to the stimuli presented to the monkey. DigiBits would not suffice. My experience with the LINC computer in the *Aplysia* experiments had demonstrated to me both its power in controlling experiments and the time required to program it, largely in machine language. I had concluded that LINC rhymed with sink because of what it was for my time. So we made it until the early 1970s without the computer. Mickey and I began trying to tame a PDP12 (half LINC and half PDP 8) to run the monkey experiment in 1972 using a program called MonkRule, and he developed a subsequent program, Monk11, when he returned to monkey work in 1975. Later we used the Real Time Experimental system (REX) that was developed for the PDP11 by Hayes, Optican, and Richmond (1982), but in the field there were almost as many systems as there were awake monkey laboratories. The use of on-line computers has made possible the sophisticated paradigms to study behavior that are used today. The drop in computer prices, from 20K for the basic PDP11 to 2K for a basic PC, has reduced laboratory setup for awake monkey recording from extensive control and analysis hardware to the installation of a set of software programs.

One of the most costly aspects of recording from awake trained monkeys was that going to a new area of the brain usually entailed initial short periods of recording followed by weeks waiting for histology to verify the site of recording. Structural imaging of the brain using magnetic resonance imaging (MRI) has allowed localization to be at least estimated during the first experiment. While precise location still requires careful histology, the MRI has become the GPS for exploring new brain areas.

Two remaining problems in single neuron recording have also been addressed by advances in neuroscience methodology. The first problem is

that while we are trying to identify a circuit within the brain of the awake monkey, this is usually not possible because we can only infer what the connections of a particular neuron are. Use of the classical techniques of antidromic and orthodromic activation of the neuron by electrically stimulating potential targets of the neuron's output or sources of its input can establish these connections before further experiments are done. We have used these techniques between the basal ganglia and the SC (Hikosaka and Wurtz, 1983d), the SC and frontal cortex (Sommer and Wurtz, 2004a), and the SC and visual cortex (Berman and Wurtz, 2010).

The second problem is related to one of the major methods of studying the brain: the analysis of behavioral deficits following brain lesions, which can be used to extend the relation of neurons to behavior beyond just a correlation. A problem with this technique, however, is that the behavior studied is both the result of the lesion and the compensation within the brain for that lesion. But the use of transmitter agonists and antagonists that reversibly inactivate or activate a region of the brain (for example, bicuculine and muscimol for GABA receptors) allows analysis of behavior within minutes of activation or inactivation, a time short enough to minimize any compensation. For example, ablation of the SC led us to conclude that the SC made minimal contributions to the guidance of saccades when the saccades were measured the day after the lesion (Wurtz and Goldberg, 1972b), but with SC inactivation with muscimol and saccades measured within minutes, deficits in saccade generation clearly were evident (Hikosaka and Wurtz, 1985). The possibility of activation and inactivation on a trial-by-trial basis (Chow et al., 2010; Han et al., 2009) would make this approach even more powerful. But even with current techniques, the combination of knowing the correlation of a specific set of neurons to behavior, and the ability to then perturb them to test any behavioral change, is one of the reasons the awake monkey technique has become one of the most powerful approaches in systems neuroscience. It is immensely satisfying to see whole sessions at the Society for Neuroscience meeting devoted to experiments on a functioning visual system, what I would refer to as active vision.

The Laboratory of Sensorimotor Research (1978–present)

In 1978 Carl Kupfer, the director of the National Eye Institute at the NIH, raised the possibility of a new laboratory within the NEI that studied the visual and oculomotor system in the best animal model of those systems, the old world monkey. Such a laboratory would collaborate with the neuroophthalmology branch of the NEI. The director of that branch was David Cogan, who had retired from Harvard and moved to the NEI, and I know that his interest in a collaborating monkey and clinical laboratory was a key factor in developing our new laboratory. But the lynchpin was Carl's view of the relation of the NEI to vision research, namely, that the Institute would

support research at all levels of the visual pathway, not just the eye as the Institute's name implied. This attitude provided the substantial and sustained support for study of the brain that led to the explosion of basic knowledge about visual and oculomotor processing in the brain beginning in the 1970s.

It might be worth mentioning the advantages of a laboratory in the NIH intramural research program. The first is the obvious one of freedom from the grant cycle. Early on I became convinced that the intramural program provided support for exploration and the accompanying failures that the grant system did not. This was brought home by serving a full term on a study section; the proposals were incredibly conservative and the criticisms were frequently technical and mundane. I concluded that the best system is the retrospective one of the intramural program: what have you done with the support you have had? This decision is based on fact and enforced by regular reviews. In contrast, the grants system is based on proposals for future discoveries with a nod to reality in the requirement for preliminary data showing that the experiment has already been done. The second is the freedom to structure your own time. Lack of teaching and committee responsibilities allows for concentration on a problem and organizing your own time that for me has been liberating. The third is the ability to bring together a group of scientists interested in the same field of work. This is much more difficult at a university because of the demands of expertise for teaching across many areas.

The timing of the new laboratory was determined by the impending completion of a new wing in the NIH clinical center that would provide the NEI with new space in close proximity to the eye clinic. The Laboratory was formally in place on October 1, 1978, with one member, me, and no space other than what Dr. Tasaki and NIMH could afford to loan me. I chose the name Laboratory of Sensorimotor Research because I thought the name was broad enough to encompass what we would want to do, and the acronym LSR had a nice ring to it. For well into 2 years as the laboratory developed we would struggle with space, until our laboratory area in the new building was completed. Making appointments also proved challenging because NIH salaries were low, and only those already working for the government, or too young to know better, were candidates. I first managed to recruit Mickey Goldberg and David L. Robinson, who had a laboratory on the Navy Medical Center Campus across the street from the NIH. Lance Optican came after a fellowship with Fred Miles in Evarts NIMH Laboratory as a theoretical biologist, and then Fred Miles himself came as well. That completed the initial scientific staff; the expectation of hiring a neuroanatomist and a psychophysicist was never carried out.

There were two basic principles for the laboratory. First, each investigator did what he wanted to do; they had already demonstrated they could pick interesting directions. I have on occasion flattered myself that I had

organized a laboratory the way one of my scientific heroes, Steve Kuffler, had done at Harvard: hire the best scientists possible and then let them alone. Second, while each of the investigators had their own laboratory rooms, all of the rest of the supply and equipment funds were pooled and distributed as needed. What sounds like a recipe for conflict turned out to give us all resources we were unlikely to have had as individuals. The give and take that was necessary for the system to work functioned flawlessly, not because it was a good system, but because of the good will and respect the investigators had for each other. In the 24 years I was Chief of the lab, I never experienced an angry encounter, and this among highly competitive scientists who were going to figure out how the brain works.

Once we were in our permanent space, I thought the LSR ran smoothly. What did not run smoothly was the planned interaction with the clinic. We all admired David Cogan, a wonderful person, a scholar of the visual and oculomotor system, an astute clinician, and endlessly helpful. One amusing case of his help was when Barry Richmond and I were doing retrobulbar blocks to paralyze a monkey's eyes in a critical experiment on the origin of an SC input (Richmond and Wurtz, 1980). In order to eliminate any distress to the monkey we would briefly anesthetize it with gas through a face mask. David laughed when he saw it. He showed us how in patients one just held the eye lid closed, passed the needle through the locally anesthetized lid, and then injected the anesthetic in the back of the orbit. But the more extended interaction between the LSR and the clinic never developed. I think it was in part due to the friction of rubbing together two different ways of doing science: we in the LSR used quantitative measures of eye movements and neuronal responses, and we verified results by repeated experiments; David took videos of a patient's eye movements and frequently based his striking insights on a single patient. There were a number of joint projects done between clinic and lab, but I feel to this day that I let down David (and Carl Kupfer). This did not dampen David's personal generosity, and he remained a warm friend and trusted mentor until his death in 1993.

I think the research laboratory is one of the wonders of science. It provides facilities that are adequate to translate ideas into experiments. More important, it provides a community of scientists who not only share technical advances but evaluation of research in the field and criticism of the work of their colleagues. The LSR has for me provided these benefits, particularly the direct criticism of experimental plans or results in lab lunches and seminars. I regarded the criticism as pointed but polite, but most postdoctoral fellows would agree that giving a practice neuroscience talk in the LSR was much more harrowing than at the meeting itself. The 15-minute practice talk routinely generated an hour of suggestions and even disagreement among suggestions. Both the investigators themselves and the spirit of the lab I think contributed to attracting truly outstanding post-doctoral fellows, which of course just further enriched the interaction within

the lab. I would be leaving out a key factor in my scientific life, if I did not acknowledge the enormous benefit I have derived from the LSR in particular and the NIH Intramural Research Program in general over 45 years. In that entire period I have never been told what to do, have been adequately supported, and have had a stream of talented fellows and supportive colleagues.

At the outset I never conceived of setting up a laboratory as something I would regard as one of my life's achievements, but the way it has turned out, and with the scientists it has attracted as staff and as fellows, I certainly do now. I resigned as Laboratory Chief in 2003, with few qualms because of the confidence in my successors, Lance Optican and then Bruce Cumming.

During the organization of the LSR, I was also preoccupied with my two teenage children who were living with me during a period of separation and divorce from my wife Sally. Several years later, however, a happy event came my way when I developed more than a friendship with Emily Thach. After commuting for many months between St Louis and Bethesda, she moved to Bethesda with her daughter Sarah and her twin sons, Will and Jim. We were married shortly later and Emily has been the light of my life for the last 30 years.

Threads of Research at the National Institutes of Health (1972–2010)

My research was guided by a conviction that using the classical distinction between the visual and motor systems was an anachronism simply because a primate's normal vision did not exist without eye movements. The visual-motor system was what I planned to study, but the field remained divided and the visual researchers regarded me as an oculomotor guy and the oculomotor types regarded me as an interloper from vision. Both were right. My view, however, was liberating and led me to follow a variety of problems on the visual-motor system. The unifying theme is that they all explored the neuronal basis of active vision, that is, the integration of the visual, oculomotor, and cognitive functions underlying visual perception and visually guided behavior. I did not, however, follow one problem to completion and then start another. I rarely felt that I had fully answered the question I set out to study and, at the end of an experimental phase, I frequently either did not know quite what to do next, knew what needed to be done but could not do it, or saw opportunities to ask questions on other problems that I thought were more exciting. The latter case was frequent because the technique of studying neurons in the functioning brain was just opening up and the primate has a very big brain.

Another factor was that, beyond my initial experiments on V1 cortex, I collaborated with postdoctoral fellows. The experimental problems

I addressed were obviously influenced by the interests of these fellows, and this also produced some shifts in direction. I have had only a small number of fellows (between one and five) working with me at any one time. I learned early on that even though my resources increased, my brain stayed the same size. A small group remained optimal. I have been unbelievably fortunate to have had such a series of bright, energetic, hard-working, young scientists come to my laboratory. I have been careful not to dispel the illusion that they are learning from me, when in fact I am getting new ways of doing things and continuing stimulation from them. What I officially do is now called mentoring. What I actually do is design and do experiments with the fellows and we both learn, as Tasaki would say, from Professor Monkey.

In the remaining part of this commentary I would like to recount a few of the experimental lines I have pursued with these wonderful fellows. I am probably already exceeding the patience of even the most enthusiastic reader, so I will concentrate on a few of the more extended threads, which means omitting many experiments. This means that some of my collaborators are not adequately represented, not because their findings were not significant, but simply because the experiments do not fit into the few threads I have space to recount. I compensate for these omissions only partially by taking this opportunity to list my postdoctoral collaborators:

| | | | |
|------------------|-----------|-------------------|--------------|
| Michael Goldberg | 1969–1972 | Charles Duffy | 1988–1993 |
| David L Robinson | 1971–1975 | Douglas Munoz | 1989–1992 |
| Charles Mohler | 1972–1976 | Gregory Recanzone | 1991–1994 |
| Joan Baizer | 1973–1976 | Hiroshi Aizawa | 1992–1996 |
| Charlene Jarvis | 1974–1975 | Satoshi Eifuku | 1994–1997 |
| Barry Richmond | 1976–1979 | Michele Basso | 1995–2000 |
| Stuart Judge | 1976–1979 | Richard Krauzlis | 1996–1998 |
| Joanne Albano | 1977–1983 | Marc Sommer | 1996–2005 |
| Okihide Hikosaka | 1979–1982 | Martin Pare | 1996–2000 |
| William Newsome | 1980–1984 | Douglas Hanes | 1997–2000 |
| Akichika Mikami | 1982–1984 | Nicholas Port | 1998–2005 |
| Max Dursteler | 1983–1986 | Stefano Ferraina | 1999–2001 |
| Hidehiko Komatsu | 1985–1988 | James Cavanaugh | 2000–present |
| David Waitzman | 1986–1990 | Kerry McAlonan | 2001–present |
| Dwayne Yamasaki | 1986–1991 | Hiroyuki Nakahara | 2002–2004 |
| Jean-Pierre Roy | 1987–1989 | Rebecca Berman | 2005–present |
| Terrence Ma | 1987–1990 | Wilsaan Joiner | 2007–present |

Saccadic Suppression

I had not found evidence for saccadic suppression in V1 neurons; they did not distinguish between nearly identical stimulus motion across a receptive field during fixation and similar stimulus motion produced by saccades. In contrast in the SC, Goldberg and I had found that some of the visual neurons showed a striking suppression of visual responses with saccades. David Lee Robinson and I verified this suppression of the visual response (Robinson and Wurtz, 1976), and we concluded that in the SC there was indeed the suppression I had expected to find in V1 cortex, and this brought some closure to the saccadic suppression search.

By the spring of 1975 I was anxious to take a break after nearly 10 years of recording in awake monkeys. It had been clear to me that I needed more knowledge of human perception and psychophysics to allow me to devise tests that measured perception in monkeys. This in turn would allow me to compare the neuronal activity I could now record in awake monkeys with their behavioral reports using the techniques of psychophysics. The NIH did not routinely offer sabbaticals; we were regarded as being on sabbatical all the time. A senior NIMH scientist, however, had canceled his plans for a sabbatical, and the opportunity was offered in the spring of 1975 to anyone who could start that summer. I had met Fergus Campbell, a psychophysicist at Cambridge University, a year earlier, he was willing for me to join his laboratory, and I arrived there in August 1975.

Cambridge was a major center for both visual physiology and psychophysics. The research roster in addition to Fergus included William Rushton, Horace Barlow, John Robson, Colin Blakemore, John Mollen, Michael Morgan, Oliver Braddick, Roger Carpenter, and David Tolhurst. Many showed up for afternoon tea with invariably interesting discussion and occasional cutting interactions in the finest English academic style. I expected to do psychophysics on Fergus's specialty, visual spatial frequency, but when we talked about experimental directions, Fergus expressed interest in studying, of all things, saccadic suppression. We did, and over a year we did a variety of pilot experiments, interspersed with an endless stream of Fergus's amusing anecdotes. After many false starts, we came to the conclusion that the suppression was heavily dependent on the visual masking of the clear visual image before and after the saccade acting on the blur during the saccade (Campbell and Wurtz, 1978). This was consistent with my failure to see active modulation in V1 and with previous work on masking (Matin et al., 1972).

My goal for the year had been to become knowledgeable and competent with psychophysical techniques and analysis. I failed on all counts. Partly this was due to the nature of the exploratory experiments we did and Fergus's seat-of-the-pants approach, which was fun, but not the methodological experience I needed. More disruptive for my plans was the separation from

my wife Sally that began when she moved to London as I stayed in Cambridge with Bill and Erica. Bill prospered during the year, but Erica missed her friends at home.

When I returned to Bethesda, Barry Richmond and Stuart Judge joined me, and we looked to see whether there was any indication of a masking effect in either V1 or SC. We found that there was and that it was strong enough to eliminate all but the strongest visual responses in V1 (Judge et al., 1980b). We also investigated whether the suppression we had seen previously in the SC visual neurons might be the result of some input from outside the visual system. One such input is referred to as a corollary discharge (Sperry, 1950) that is a signal sent from regions of the brain that generate a movement to other brain regions in order to inform those regions that a movement is about to occur. This corollary discharge could produce the suppression in the SC, but suppression could also have resulted from proprioceptive input from the eye muscle contraction. Barry and I addressed this issue by blocking eye movements (using Cogan's retrobulbar block method) in order to reduce proprioception. The monkey should still be trying to make saccades, which would produce a corollary discharge, and we could see that it was doing so from the bursts of activity we recorded from eye muscle motor neurons. We found that suppression in the SC persisted and concluded that the SC visual suppression must be the result of a corollary discharge (Richmond and Wurtz, 1980), possibly from the saccade neurons in the SC intermediate layers (Lee et al., 2007).

I initially thought that saccadic suppression was a simple phenomenon that would be easy to investigate at a neuronal level. It was not. I think our long series of experiments show that the suppression results from both visual masking and a corollary discharge, and both factors operate at multiple levels along the visual pathways (Wurtz, 2008). This provides an exceptionally clear example of a seemingly simple cognitive phenomenon that is indeed served by simple brain mechanisms, but there are multiple such mechanisms and they act at multiple levels, a distributed modulation.

A Corollary Discharge to Frontal Cortex

The suppression of vision during saccades is an important mechanism for our normal vision, but the major issue is why our perception of the visual world does not appear to jump as the image on the retina does with each saccade. The classical explanation of von Helmholtz (1925) is that an "effort of will" informs the visual system of the impending saccade, the same idea as the corollary discharge of Sperry described earlier or the efference copy of von Holst and Mittelstaedt (1950). While Richmond and I were convinced in 1980 that we had seen the suppressive action of a corollary discharge acting on SC visual neurons, we had seen no evidence of the corollary itself. Identification of a corollary discharge in the primate brain remained largely hypothetical.

This changed after an astute observation by Marc Sommer (1998). Marc, along with Martin Pare and Stefano Ferraina, was testing whether we could identify a single final output signal from frontal and parietal cortex to the SC (Wurtz et al., 2001). We used antidromic stimulation from the colliculus to selectively activate the cortical output neurons with the expectation that we could thereby determine which signals (visual, visual-motor, motor) in frontal and parietal cortex were the final output signals. To my chagrin, all were represented in the output, which meant that we could not determine what the cortical processing had accomplished by looking for a single final output. Marc noticed, however, that in the frontal eye field area of frontal cortex, antidromic response was frequently followed by a later response that could be shown to be an orthodromic response from the SC to frontal eye field (Sommer and Wurtz, 1998). This led to identifying a relay in this pathway in a tiny area of the medial dorsal nucleus of the thalamus. The characteristics of the signals in the pathway and the consequences of its interruption for the control of saccades convinced us that we had at last identified a corollary discharge in the primate brain and one that went to cerebral cortex (Sommer and Wurtz, 2002; 2004a; 2004b).

The next issue was whether this pathway might contribute to our perception of visual stability during saccades by in some way countering the displacement of the image that occurs with each saccade. Without going into details, Goldberg and his collaborators (Duhamel et al., 1992; Umeno and Goldberg, 1997) had shown that there were neurons in parietal and frontal cortex whose receptive fields shifted in anticipation of an upcoming saccade. They suggested that this represented a “remapping” of the visual field with each saccade that might underlie our perception of visual stability. The remapping hypothesis required the input of a corollary discharge for saccades, and the obvious question was whether our corollary discharge was the one required by the shifting RFs. This question could be answered by inactivating the relay and seeing whether the shifts of the frontal eye field RFs were reduced. They were and this heroic experiment indicated that the corollary discharge might provide a necessary input for visual perception as well as for movement (Sommer and Wurtz, 2008; Wurtz, 2008). A key remaining question is whether the shifting RFS are related to stable visual perception, but all the techniques are available to answer that question.

So the corollary discharge, which had eluded me in my initial experiments on V1 cortex many years earlier, was found to project to regions of frontal cortex from layers in the SC via a pathway through thalamus, all of which were not even recognized when I was looking at V1. To me it is a striking illustration of how the success of asking questions about higher level functions depends on what is known about the basic organization of a system within the brain. The right question asked at the wrong place is one of the mistakes I think I have made most frequently. But it is rare that information about a brain system is sufficient to indicate in advance all the

functions the system performs and what questions it is sensible to ask. I am quite sure hindsight will show I am continuing the same mistakes now.

Spatial Attention

Mickey Goldberg and I had established an enhanced visual response when the stimulus activating a superficial layer SC neuron became the target for an upcoming saccade. We suggested that this might be a possible correlate of attention. We had no measure of attention, however, and the argument was a logical one: saccades are made to visual targets and a shift of attention precedes saccades. We had found presaccadic activity in one SC layer and the enhanced visual response in the adjacent visual layer, so all the machinery for saccadic activity to act on visual activity was in adjacent layers. It was a controversial idea at the time, but it was also an experimental demonstration of a neuronal process that might underlie a major cognitive process, visual spatial attention. It also generated amusement; at one oculomotor after-dinner entertainment, visual enhancement was represented by a padded bra. Nonetheless, over the next several years we evaluated the enhancement, that is, the neuronal one.

Chuck Mohler and I first investigated how closely related the enhancement was to saccade generation. We found that the enhancement became larger as the saccade onset came closer to the time of target onset. This was consistent with saccade preparation being the source of the visual enhancement and with it reaching the SC superficial visual cells by an ascending projection from the intermediate layer, saccade-related neurons (Wurtz and Mohler, 1976b). We also tested whether the enhancement was more prominent when the monkey responded to the stimulus with a saccade as opposed to a hand movement during continuing fixation, at last studying my first trained monkey, Ethel. The enhancement was reduced with no saccade, and we concluded that the SC enhancement was better regarded as movement preparation rather than attentional shift (Wurtz and Mohler, 1976b). We also found that neurons in the frontal eye field showed stronger enhancement with saccades (Wurtz and Mohler, 1976a), but Bushnell, Goldberg, and Robinson (1981) later found that the enhancement in parietal cortex was present with or without saccades. This led to our generalization that parietal cortex was related to attention but that SC and frontal eye field were more closely related to saccade preparation (Wurtz et al., 1980; 1982).

The flaw in our conclusion was that we assumed that when the monkey did not make a saccade there was no preparatory activity for a saccade because no saccade was made. Subsequent experiments, however, showed that some SC saccade-related neurons we later referred to as buildup neurons began to discharge long before the saccade (Mohler and Wurtz, 1976; Munoz and Wurtz, 1995a) and did so even if the saccade was not actually made. In addition, the subsequently developed motor theory of attention

(Rizzolatti, 1983) and the much later experimental support for it from experiments using covert shifts of attention (Moore et al., 2003) renewed the possibility that the neuronal mechanisms underlying visual spatial attention overlapped those for the preparation to make a saccade. This in turn raised the possibility that the now prevalent finding of neuronal modulation with attention in visual cortex could result from an input related to saccade preparation, including that ascending from SC. James Cavanaugh and I therefore tested the effect on attention by activating SC and testing the effect on visual motion processing that is likely to be restricted to cortical processing. We produced a shift of attention by a visual cue and also by low-level SC stimulation that did not evoke a saccade (Cavanaugh and Wurtz, 2004), as did a similar experiment from Bill Newsome's laboratory (Muller et al., 2005). Later experiments suggested that the shift was not the result of attempting to look at a stimulation-produced visual phosphene (Cavanaugh et al., 2006). The satisfying aspect of these later experiments was that the mechanism of spatial visual attention, at least in some cases, might result simply from input from saccade preparation. The less than satisfying aspect is that we should have done the experiments at least 20 years earlier.

The possibility that ascending activity could produce attentional modulation also suggested that the projection from the SC to the thalamic reticular nucleus might modulate the retinal-cortical pathway via its projection to the lateral geniculate nucleus. Such an action of the thalamic reticular nucleus had been suggested by Francis Crick in his spotlight of attention hypothesis (Crick, 1984). Kerry McAlonan and Cavanaugh showed that both the reticular neurons and the LGN neurons were modulated with attention in ways consistent with the reticular neurons acting on the LGN (McAlonan et al., 2008), but whether this is related to the preparation to make saccades remains unknown.

Finally, we had good reason to believe that the SC was involved in target selection, since ablation had been shown to produce neglect in the contralateral visual field (Albano and Wurtz, 1978). Later experiments with Michele Basso showed that activity in the SC during target selection varied with the conditions of the selection: the amplitude of the buildup activity was increased as the certainty that a stimulus would be the target of the saccade increased (Basso and Wurtz, 1997; 1998).

The results of this series of experiments, widely spaced over time, supports the idea that the SC provides ascending signals that contribute to shifts of spatial attention, and clearly demonstrate that changes in the SC are integrally involved in target selection. This has become abundantly clear from other recent work (Keller et al., 2005; Lovejoy and Krauzlis, 2009). The major point, however, is that seeing the modulation of visual responses first in the SC visual cells and then in many cortical areas, and the possibility that this modulation may be related to the preparation to make a saccade,

provides hope that cognitive processes may be understandable on the basis of simple neuronal circuits.

SC and the Basal Ganglia

After identifying types of neurons and layers of organization in the SC in the early 1970s, one of the obvious next steps was to try to use the SC to identify the larger circuits in the brain of which the SC was just one node. There were two ways to go: downward to see how the SC output was converted into the movement signals to produce saccades, or upward to see how the input to the SC influenced its activity. The downward direction was attractive because it would connect the map in the SC to the activity of neurons in the brain stem that decreased or increased their discharge before saccades. This direction also was particularly attractive because Okihide Hikosaka was coming to the lab, and he had completed elegant studies in the cat on one of the key brainstem neurons that the SC might act on, the inhibitory burst neurons. The drawback was that to be most informative the exact connections between the SC and these neurons would need to be worked out, and this seemed to be a daunting task. In contrast, a major input to the SC was from the basal ganglia. This input was unexplored, and if I looked on the study of the awake monkey as a window on cognition at higher levels in the brain, going upward to the basal ganglia made sense. This logic of stepping backward in the saccadic system is analogous to stepping forward in the visual pathway; it is just that we were starting near the end rather than near the beginning of the visual-motor pathway.

Okihide and I concentrated on the input from the basal ganglia to the SC. This arises in the substantia nigra pars reticulata which had recently been shown to have inhibitory input to the SC. Our first observation was that the pars reticulata neurons had high discharge rates and that they usually paused before saccades, just the inverse of what SC neurons did. This was, however, exactly what we would expect if the input to the SC was inhibitory because the pars reticulata pause would release the SC from inhibition just before the burst of the saccade-related neurons in the SC. We concluded that the SC was driven by a push-pull mechanism of excitation from one input (including that from the frontal eye field) and release from inhibition from the other input, the pars reticulata of the basal ganglia. It also became clear that the pause in activity in the pars reticulata varied with the behavioral conditions under which the saccade was made. For example, many pars reticulata neurons did not pause with saccades to plainly visible targets, but paused only with saccades guided by memory to the location of a previously flashed target. This led us to suggest that the basal ganglia might control movement from stored information, or more generally, with movements that could be regarded as voluntary (Hikosaka and Wurtz, 1983a; 1983b; 1983c; 1983d).

We also used two techniques, whose use in awake monkeys was novel at the time, in order to further establish the connection between the pars reticulata and the SC. The first was stimulation in SC to antidromically activate neurons in pars reticulata that project to SC. Here we expanded its use to determine where the axons terminated in the colliculus, and found low current threshold activation among the saccade neurons in the SC intermediate layers. The second technique was the local inactivation of the neurons we had studied in order to see if their absence or hyperactivity produced any behavioral changes (Hikosaka and Wurtz, 1985). We were able to mimic the tonic inhibitory effect of the pars reticulata on the SC by injecting an inhibitory transmitter agonist into the SC (the GABA agonist, muscimol) and reducing the inhibitory input with an antagonist (bicuculline). The inactivation of the SC in the awake monkey and the immediate monitoring of behavioral changes also revealed more dramatic deficits in saccade amplitude and velocity than Goldberg and I had seen on the day after an SC ablation. This suggested that the lack of a more severe deficit in the original experiments was the result of a recovery that had occurred between ablation and behavioral test.

Our work on the relation of the substantia nigra pars reticulata output of the basal ganglia as assayed in the SC was one of the first attempts to study the relation between two successive steps in a visual-motor brain circuit, in this case the circuit for controlling saccades. We were able to do so by using a trilogy of techniques: the relation of the neurons in the two structures to saccades, the connection of the neurons in the two structures by antidromic stimulation, and the effect of activation/inactivation of either structure on saccade generation. While there were obviously substantial limitations to what we could conclude, I think we demonstrated that the techniques needed to begin to dissect these circuits in the brain were now available.

Visual Motion in Awake Monkeys

After my initial forays into V1 cortex, the areas beyond V1 began to be identified (Zeki 1975), and I had the opportunity to investigate one of these areas, MT, when Bill Newsome came to the lab in 1980. Bill had investigated MT with John Allman and then David van Essen in the anesthetized monkey, and with Aki Mikami and Max Dursteller we explored MT in the awake monkey for the first time. We verified the expected directional selectivity for motion (Mikami et al. 1986a), and then went on to test the relation of MT neurons to apparent motion, the motion produced by successive flashes (the phi motion of the movies). We found that MT directionally selective neurons had the appropriate spatial and temporal properties to underlie one type of apparent motion seen in humans, the short range process (Braddick 1974), which was not the case for V1 neurons (Mikami et al. 1986b; Newsome et al. 1986).

Thus we had established that MT neurons could underlie the perception of apparent motion in ways that V1 could not. What we had not done was take the next step of showing that ablation within MT altered the monkey's perception of apparent motion. This soon became possible because in our next experiments we developed a method for selectively ablating small regions of MT.

At the time of these experiments, the early 1980s, one of the major questions about cortical visual processing was whether different types of processing such as color, form, and motion, were represented differentially in separate extra-striate areas. Therefore, if motion were represented primarily in MT, and we ablated MT, we would expect to see a deficit in a behavior that depended on motion. We used a task that required the monkey to make a saccade to and then pursue a moving target because we could quantitatively measure the pursuit movement of the eye that precedes the saccade to the target. We made ibotenic acid lesions in MT affecting just one region of its retinotopic map of the visual field. We found a deficit in the use of the target moving in the visual field represented by the ablated MT (Newsome et al. 1985). The deficit was specific for the use of motion and not position, and I think this was one of the first behavioral demonstrations of dedicated processing in a specific extrastriate area (Newsome and Wurtz 1988). This was of course a demonstration related to eye movements, and Bill went on in collaboration with Tony Movshon to show the relation of MT to the perception of visual motion. My failure to move promptly to perceptual deficits following inactivation of MT was a carry over of my failure to integrate psychophysical techniques and thinking into my plans after my time at Cambridge.

Subsequent experiments explored the extent of the contributions of both MT and the next visual motion area, MST, to the control of pursuit eye movements. We first found that the ibotenic acid lesion of MST produced a deficit in the maintenance of pursuit for targets moving toward the side of the lesion (Dürsteler et al. 1987). This was exactly the deficit seen in humans with cortical lesions, and we suggested that we had located the level of visual processing that leads to that deficit. Work with Hidehiko Komatsu also showed that MST was probably a group of areas. One, a lateral-anterior area (MSTl) that represented regions close to the fovea, was related to pursuit maintenance and, when electrically stimulated, altered pursuit. Another, a dorsal-medial area (MSTd) was more responsive to full field visual stimulation (Komatsu and Wurtz 1988a; Komatsu and Wurtz 1988b).

When Charlie Duffy came to the lab we investigated whether the large fields of MSTd might be the area that responded to large field optic flow patterns, the patterns that are generated as we walk through our environment, and that Gibson (1954) had emphasized as critical for perception and movement. The neuronal responses in the area indicated that MSTd was such an area (Duffy and Wurtz 1991a; 1991b), as predicted by previous experiments

using looming stimuli (Tanaka et al. 1986). Further experiments showed the types of flow stimuli that activated these neurons, and that the response of some neurons to the direction of stimulus motion depended upon the depth of that motion in the visual field as determined by their binocular disparity (Roy and Wurtz 1990).

When I was first recording from V1, I met James Gibson at Cornell and he urged me to use more than just spot and slit stimuli. But I could not see how the small V1 RFs could possibly respond to the large field optic flow Gibson was interested in. These studies in MSTd many years later revealed at last the types of neuronal responses Gibson had told me must be there, and so it was gratifying to find them even though it was too late to show them to him.

Our experiments in MT and MST were among the first to show the relation of the areas to perception (apparent motion), to the control of movement (smooth pursuit), the response to optic flow, and the response to disparity stimuli. These are lines that I have not followed beyond these initial experiments, but my collaborators obviously have done so with much sharper questions, better methods, and immense success.

The Function of Superior Colliculus Neuronal Elements

Most of my experiments have used the SC as the starting point for exploring the cerebral cortex by looking at the inputs from frontal and parietal cortex to SC (Wurtz et al., 2001), and the ascending pathways that modulate cortex via the thalamic medial dorsal or pulvinar nuclei (Berman and Wurtz, 2010; Sommer and Wurtz, 2008). What further exploration of the SC I did, after it burst on the scene in the early 1970s, was embedded in a much larger effort by a number of laboratories, particularly that of David Sparks.

Most of everyone's effort was devoted to the saccade-related neurons in the intermediate SC layers. A significant advance in sorting out the types of saccade related-neurons followed the arrival of Doug Munoz who had studied the SC in cats with Dan Guitton (Munoz and Guitton, 1991; Munoz et al., 1991). In the monkey, the neurons with a burst of activity just before the saccade had been the center of interest. Other largely unstudied neurons, however, began to increase their activity hundreds of milliseconds before the saccade and frequently had little burst activity. We referred to these descriptively as buildup neurons (Munoz and Wurtz, 1995a) and, as I have already mentioned, I think the early activity of these neurons make them prime candidates for producing the modulations of activity in other layers of the SC and in other areas of the brain related to saccades.

Another finding derived from the cat investigations was the identification of "fixation neurons" in the rostral SC that represents the central visual field. Instead of becoming active before saccades, they became active when the monkey fixated (Munoz and Wurtz, 1993a). Because of their characteristics

we considered them to be rostral extensions of the buildup neurons, but because when we inactivated them the monkey made irrepressible saccades and when we activated them there was prolonged fixation (Munoz and Wurtz, 1993b), we referred to the area as a fixation zone. Subsequent work of Rich Krauzlis and Michele Basso (Krauzlis et al., 2000; 1997) showed that these neurons might provide a position error that could be used either for saccades or smooth pursuit. Later work from Krauzlis's lab showed that the rostral SC neurons were active before microsaccades in ways similar to the ways in which the rest of the SC became active before larger saccades (Hafed et al., 2009). This and other findings led to the view that these rostral neurons were the same as more caudal buildup neurons; they all inhibited activity in other SC areas when they were active. Activating or inactivating these rostral SC neurons did modify fixation and this must occur when the rostral neurons are active, but they are not a separate type of SC neuron, just a rostral extension of the buildup neurons as we recognized from the outset. Our use of the terms *fixation neurons* and *fixation zone*, with the benefit of hindsight, was less than optimal.

Another hypothesis based on the SC of the cat was that the duration of activity and thus the amplitude of a saccade was the result of a wave of activity that moved across the SC. In Doug Munoz's recording from the monkey we saw not a wave but a spread or expansion of activity during a saccade (Munoz and Wurtz, 1995b). The sequence could be seen even more clearly by recordings at two SC sites (Port et al., 2000). I thought this was potentially a beautiful illustration of how activity across a map of movement could control the metrics of a movement. The characteristics of the spread, its timing, and other factors, however, made the proposal controversial, to say the least. The experimental result that convinced me that the activity did *not* control the amplitude of the saccade was that, when the spread was disrupted and presumably slowed by muscimol inactivation of the SC midway along the retinotopic map, the saccades did not become longer as predicted by a slower spread, but stayed the same or became shorter (Aizawa and Wurtz, 1998; Quaia et al., 1998). This left the observation of the spread a valid one in my view, but without a function. Hiro Nakahara had the idea that the spread was the inevitable result of the distortion of SC movement fields that results from the constriction of the magnification factor with eccentricity, and a simulation of a model produced results similar to our SC observations (Nakahara et al., 2006). I now think of the spread as a classic biological epiphenomena in that it directly results from the organization of a biological structure but does not indicate the function of the organization.

The SC would be one of the best understood regions of cerebral cortex, that is, if it were in cerebral cortex. With a layered structure, a retinotopic map, a limited number of neuron types, and the ability to quantitatively measure the eye movement behavior it controls, the SC has evolved into an ideal structure for modeling the transition from sensory input to movement

output (Quaia et al., 1999; Wurtz and Optican, 1994), including its role in attention and target selection (Krauzlis et al., 2004). The SC also serves as the best window onto the transition from cerebral cortical processing for behavior to the brainstem execution of that behavior. More recently, the SC has begun to provide the first insights into what information the brainstem feeds back to the cerebral cortex.

Conclusion

In writing this I have had the disconcerting realization that I have been studying brain and behavior for over half a century, starting in 1958 in the laboratory of Jim Olds. The changes in studying systems in the brain over that time are staggering. Then, the relation of brain activity to behavior was studied primarily using the electroencephalogram (EEG). The EEG was a filtered electrical signal averaged over many thousands of neurons. Occasionally animals were trained, but only in simple conditioning tasks. Now in contrast, activity of individual neurons can be correlated with highly sophisticated behavioral tests.

Put another way, the questions have not radically changed, but the experimental power to answer them has. Fifty years ago, if we had questions about simple behaviors such as the generation of movement or about cognitive processes, such as attention and perception, we could not go into the brain and explore the neuronal activity contributing to these functions. Now we can record from single neurons in identified brain structures and measure how well their activity correlates to even cognitive behavior. We can then go beyond this correlation of neurons and behavior by selectively activating or inactivating local groups of neurons, and measuring how the behavior changes. Finally, by determining what neurons in one brain area are functionally connected to those in another area, we can at least begin to outline the circuits in the brain producing behavior. We can begin to see the neuronal *mechanisms* underlying behavior, not just the correlations.

If we judge success by how far our understanding of the brain has come compared to where we were 50 years ago, we have had stunning success, far beyond anything I could have imagined. But if we judge by how far we have to go, the challenge is immense and sobering. The challenge may be matched, however, by the emerging new techniques for studying hundreds of neurons at a time, knowing their types and connections, and manipulating their activity millisecond by millisecond. While the last 50 years have been exciting times for studying the brain, and it is an incredible gift to have participated in it, I envy those starting to study the brain now.

I am obviously expressing my view through my tiny window onto just one segment of neuroscience, systems neuroscience, and even then onto just the system I have studied. A universally recognized change, however, is that there is now a field called neuroscience. Particularly since the founding of

the Society for Neuroscience in 1969, the multiple approaches to the study of the nervous system are recognized as parts of a common goal of understanding the brain and the behavior it produces. Students now need not apologize for studies in what used to be disparate areas but are now encompassed by neuroscience. News reports refer to neuroscience research as readily as they do to space research. I have been fortunate to have spanned this rise of neuroscience, seen its stunning advances, and contributed a bit to its development.

References

- Aizawa H, and Wurtz RH. Reversible inactivation of monkey superior colliculus. I. Curvature of saccadic trajectory. *J Neurophysiol* 79: 2082–2096, 1998.
- Albano JE, and Wurtz RH. Modification of the pattern of saccadic eye movements following ablation of the monkey superior colliculus. *Soc Neurosci Abs* 4: 161, 1978.
- Basso MA, and Wurtz RH. Modulation of neuronal activity by target uncertainty. *Nature* 389: 66–69, 1997.
- Basso MA, and Wurtz RH. Modulation of neuronal activity in superior colliculus by changes in target probability. *J Neurosci* 18: 7519–7534, 1998.
- Berman RA, and Wurtz RH. Functional identification of a pulvinar path from superior colliculus to cortical area MT. *J Neurosci* 30: 6342–6354, 2010.
- Braddick O. A short-range process in apparent motion. *Vision Res* 14: 519–527, 1974.
- Bushnell MC, Goldberg ME, and Robinson DL. Behavioral enhancement of visual responses in monkey cerebral cortex: I. Modulation in posterior parietal cortex related to selective visual attention. *J Neurophysiol* 46: 755–772, 1981.
- Campbell FW, and Wurtz RH. Saccadic omission: why we do not see a grey-out during a saccadic eye movement. *Vision Res* 18: 1297–1303, 1978.
- Cavanaugh J, Alvarez BD, and Wurtz RH. Enhanced performance with brain stimulation: attentional shift or visual cue? *J Neurosci* 26: 11347–11358, 2006.
- Cavanaugh J, and Wurtz RH. Subcortical modulation of attention counters change blindness. *J Neurosci* 24: 11236–11243, 2004.
- Chow BY, Han X, Dobry AS, Qian X, Chuong AS, Li M, Henninger MA, Belfort GM, Lin Y, Monahan PE, and Boyden ES. High-performance genetically targetable optical neural silencing by light-driven proton pumps. *Nature* 463: 98–102, 2010.
- Crick F. Function of the thalamic reticular complex: the searchlight hypothesis. *Proc Natl Acad Sci USA* 81: 4586–4590, 1984.
- Davidson RM, and Bender DB. Selectivity for relative motion in the monkey superior colliculus. *J Neurophysiol* 65: 1115–1133, 1991.
- Dodge R. The illusion of clear vision during eye movements. *Psychol Bull* 2: 193–199, 1905.
- Duffy CJ, and Wurtz RH. Sensitivity of MST neurons to optic flow stimuli. I. A continuum of response selectivity to large-field stimuli. *J Neurophysiol* 65: 1329–1345, 1991a.

- Duffy CJ, and Wurtz RH. Sensitivity of MST neurons to optic flow stimuli. II. Mechanisms of response selectivity revealed by small-field stimuli. *J Neurophysiol* 65: 1346–1359, 1991b.
- Duhamel J-R, Colby CL, and Goldberg ME. The updating of the representation of visual space in parietal cortex by intended eye movements. *Science* 255: 90–92, 1992.
- Dürsteler MR, Wurtz RH, and Newsome WT. Directional pursuit deficits following lesions of the foveal representation within the superior temporal sulcus of the macaque monkey. *J Neurophysiol* 57: 1262–1287, 1987.
- Evarts EV. Methods for recording activity of individual neurons in moving animals. In: *Methods in Medical Research*, edited by Rushmer RF. Chicago: Year Book, 1966, pp. 241–250.
- Evarts EV. Relation of pyramidal tract activity to force exerted during voluntary movement. *J Neurophysiol* 31: 14–27, 1968a.
- Evarts EV. A technique for recording activity of subcortical neurons in moving animals. *Electroencephalog Clin Neurophysiol* 24: 83–86, 1968b.
- Fuchs AF. Saccadic and smooth pursuit eye movements in the monkey. *J Physiol (Lond)* 191: 609–631, 1967.
- Fuchs AF, and Robinson DA. A method for measuring horizontal and vertical eye movement chronically in the monkey. *J Appl Physiol* 21: 1068–1070, 1966.
- Gibson JJ. The visual perception of objective motion and subjective movement. *Psychol Rev* 61: 304–314, 1954.
- Goldberg ME, and Wurtz RH. Activity of superior colliculus in behaving monkey: I. Visual receptive fields of single neurons. *J Neurophysiol* 35: 542–559, 1972a.
- Goldberg ME, and Wurtz RH. Activity of superior colliculus in behaving monkeys. II. Effect of attention on neuronal responses. *J Neurophysiol* 35: 560–574, 1972b.
- Hafed ZM, Goffart L, and Krauzlis RJ. A neural mechanism for microsaccade generation in the primate superior colliculus. *Science* 323: 940–943, 2009.
- Han X, Qian X, Bernstein JG, Zhou HH, Franzesi GT, Stern P, Bronson RT, Graybiel AM, Desimone R, and Boyden ES. Millisecond-timescale optical control of neural dynamics in the nonhuman primate brain. *Neuron* 62: 191–198, 2009.
- Hays AV, Richmond BJ, and Optican LM. A UNIX-based multiple process system for real-time data acquisition and control. *WESCON Conf Proc* 2: 1–10, 1982.
- Hikosaka O, and Wurtz RH. Visual and oculomotor functions of monkey substantia nigra pars reticulata. I. Relation of visual and auditory responses to saccades. *J Neurophysiol* 49: 1230–1253, 1983a.
- Hikosaka O, and Wurtz RH. Visual and oculomotor functions of monkey substantia nigra pars reticulata. II. Visual responses related to fixation of gaze. *J Neurophysiol* 49: 1254–1267, 1983b.
- Hikosaka O, and Wurtz RH. Visual and oculomotor functions of monkey substantia nigra pars reticulata. III. Memory-contingent visual and saccade responses. *J Neurophysiol* 49: 1268–1284, 1983c.
- Hikosaka O, and Wurtz RH. Visual and oculomotor functions of monkey substantia nigra pars reticulata. IV. Relation of substantia nigra to superior colliculus. *J Neurophysiol* 49: 1285–1301, 1983d.

- Hikosaka O, and Wurtz RH. Modification of saccadic eye movements by GABA-related substances. I. Effect of muscimol and bicuculline in monkey superior colliculus. *J Neurophysiol* 53: 266–291, 1985.
- Holt EB. Eye movement and central anesthesia. *Harvard Psychol Studies* 1: 3–45, 1903.
- Hubel DH. Single unit activity in striate cortex of unrestrained cats. *J Physiol* 147: 226–238, 1959.
- Hubel DH. Tungsten microelectrode for recording from single units. *Science* 125: 549–550, 1957.
- Hubel DH, and Wiesel TN. Receptive fields and functional architecture of monkey striate cortex. *J Physiol* 195: 215–243, 1968.
- Judge SJ, Richmond BJ, and Chu FC. Implantation of magnetic search coils for measurement of eye position: an improved method. *Vision Res* 20: 535–538, 1980a.
- Judge SJ, Wurtz RH, and Richmond BJ. Vision during saccadic eye movements. I. Visual interactions in striate cortex. *J Neurophysiol* 43: 1133–1155, 1980b.
- Keller EL, Lee KM, and McPeck RM. Readout of higher-level processing in the discharge of superior colliculus neurons. *Ann NY Acad Sci* 1039: 198–208, 2005.
- Komatsu H, and Wurtz RH. Relation of cortical areas MT and MST to pursuit eye movements. I. Localization and visual properties of neurons. *J Neurophysiol* 60: 580–603, 1988a.
- Komatsu H, and Wurtz RH. Relation of cortical areas MT and MST to pursuit eye movements. III. Interaction with full field visual stimulation. *J Neurophysiol* 60: 621–644, 1988b.
- Krauzlis RJ, Basso MA, and Wurtz RH. Discharge properties of neurons in the rostral superior colliculus of the monkey during smooth-pursuit eye movements. *J Neurophysiol* 84: 876–891, 2000.
- Krauzlis RJ, Basso MA, and Wurtz RH. Shared motor error for multiple eye movements. *Science* 276: 1693–1695, 1997.
- Krauzlis RJ, Liston D, and Carello CD. Target selection and the superior colliculus: goals, choices and hypotheses. *Vision Res* 44: 1445–1451, 2004.
- Lee PH, Sooksawate T, Yanagawa Y, Isa K, Isa T, and Hall WC. Identity of a pathway for saccadic suppression. *Proc Natl Acad Sci USA* 104: 6824–6827, 2007.
- Lovejoy LP, and Krauzlis RJ. Inactivation of primate superior colliculus impairs covert selection of signals for perceptual judgments. *Nat Neurosci* 13: 261–266, 2009.
- Matin E, Clymer AB, and Matin L. Metacontrast and saccadic suppression. *Science* 178: 179–182, 1972.
- McAlonan K, Cavanaugh J, and Wurtz RH. Guarding the gateway to cortex with attention in visual thalamus. *Nature* 456: 391–394, 2008.
- Mikami A, Newsome WT, and Wurtz RH. Motion selectivity in macaque visual cortex. I. Mechanisms of direction and speed selectivity in extrastriate area MT. *J Neurophysiol* 55: 1308–1327, 1986a.
- Mikami A, Newsome WT, and Wurtz RH. Motion selectivity in macaque visual cortex. II. Spatiotemporal range of directional interactions in MT and V1. *J Neurophysiol* 55: 1328–1339, 1986b.

- Mohler CW, and Wurtz RH. Organization of monkey superior colliculus: intermediate layer cells discharging before eye movements. *J Neurophysiol* 39: 722–744, 1976.
- Moore T, Armstrong KM, and Fallah M. Visuomotor origins of covert spatial attention. *Neuron* 40: 671–683, 2003.
- Muller JR, Philiastides MG, and Newsome WT. Microstimulation of the superior colliculus focuses attention without moving the eyes. *Proc Natl Acad Sci USA* 102: 524–529, 2005.
- Munoz DP, and Guitton D. Control of orienting gaze shifts by the tectoreticulospinal system in the head-free cat. II. Sustained discharges during motor preparation and fixation. *J Neurophysiol* 66: 1624–1641, 1991.
- Munoz DP, Guitton D, and Pélisson D. Control of orienting gaze shifts by the tectoreticulospinal system in the head-free cat. III. Spatiotemporal characteristics of phasic motor discharges. *J Neurophysiol* 66: 1642–1666, 1991.
- Munoz DP, and Wurtz RH. Fixation cells in monkey superior colliculus. I. Characteristics of cell discharge. *J Neurophysiol* 70: 559–575, 1993a.
- Munoz DP, and Wurtz RH. Fixation cells in monkey superior colliculus. II. Reversible activation and deactivation. *J Neurophysiol* 70: 576–589, 1993b.
- Munoz DP, and Wurtz RH. Saccade-related activity in monkey superior colliculus. I. Characteristics of burst and buildup cells. *J Neurophysiol* 73: 2313–2333, 1995a.
- Munoz DP, and Wurtz RH. Saccade-related activity in monkey superior colliculus. II. Spread of activity during saccades. *J Neurophysiol* 73: 2334–2348, 1995b.
- Nakahara H, Morita K, Wurtz RH, and Optican LM. Saccade-related spread of activity across superior colliculus may arise from asymmetry of internal connections. *J Neurophysiol* 96: 765–774, 2006.
- Newsome WT, Mikami A, and Wurtz RH. Motion selectivity in macaque visual cortex. III. Psychophysics and physiology of apparent motion. *J Neurophysiol* 55: 1340–1351, 1986.
- Newsome WT, and Wurtz RH. Probing visual cortical function with discrete chemical lesions. *Trends Neurosci* 11: 394–400, 1988.
- Newsome WT, Wurtz RH, Dursteler MR, and Mikami A. Deficits in visual motion processing following ibotenic acid lesions of the middle temporal visual area of the macaque monkey. *J Neurosci* 5: 825–840, 1985.
- Olds J. A neural model for sign-gestalt theory. *Psychol Rev* 61: 59–72, 1954.
- Olds J, and Milner P. Positive reinforcement produced by electrical stimulation of septal area and other regions of rat brain. *J Comp Physiol Psychol* 47: 419–427, 1954.
- Pettigrew JD, Nikara T, and Bishop PO. Responses to moving slits by single units in cat striate cortex. *Exp Brain Res* 6: 373–390, 1968.
- Port NL, Sommer MA, and Wurtz RH. Multielectrode evidence for spreading activity across the superior colliculus movement map. *J Neurophysiol* 84: 344–357, 2000.
- Quaia C, Aizawa H, Optican LM, and Wurtz RH. Reversible inactivation of monkey superior colliculus. II. Maps of saccadic deficits. *J Neurophysiol* 79: 2097–2110, 1998.

- Quaia C, Lefevre P, and Optican LM. Model of the control of saccades by superior colliculus and cerebellum. *J Neurophysiol* 82: 999–1018, 1999.
- Richmond BJ, and Wurtz RH. Vision during saccadic eye movements. II. A corollary discharge to monkey superior colliculus. *J Neurophysiol* 43: 1156–1167, 1980.
- Rizzolatti G. Mechanisms of selective attention in mammals. In: *Advances in Vertebrate Neuroethology*, edited by Ewert J-P, Capranica R, and Ingle DJ. Plenum Publishing, 1983, pp. 261–297.
- Robinson DA. Eye movements evoked by collicular stimulation in the alert monkey. *Vis Res* 12: 1795–1808, 1972.
- Robinson DA. A method of measuring eye movement using a scleral search coil in a magnetic field. *IEEE Trans Biomed Eng* 10: 137–145, 1963.
- Robinson DL, and Wurtz RH. Use of an extraretinal signal by monkey superior colliculus neurons to distinguish real from self-induced stimulus movement. *J Neurophysiol* 39: 852–870, 1976.
- Roy JP, and Wurtz RH. The role of disparity-sensitive cortical neurons in signalling the direction of self-motion. *Nature* 348: 160–162, 1990.
- Schiller PH. Some functional characteristics of the superior colliculus of the rhesus monkey. *Bibl ophthalmol* 82: 122–129, 1972.
- Sommer MA, and Wurtz RH. Frontal eye field neurons orthodromically activated from the superior colliculus. *J Neurophysiol* 80: 3331–3335, 1998.
- Sommer MA, and Wurtz RH. A pathway in primate brain for internal monitoring of movements. *Science* 296: 1480–1482, 2002.
- Sommer MA, and Wurtz RH. What the brain stem tells the frontal cortex. I. Oculomotor signals sent from superior colliculus to frontal eye field via mediodorsal thalamus. *J Neurophysiol* 91: 1381–1402, 2004a.
- Sommer MA, and Wurtz RH. What the brain stem tells the frontal cortex. II. Role of the SC-MD-FEF pathway in corollary discharge. *J Neurophysiol* 91: 1403–1423, 2004b.
- Sommer MA, and Wurtz RH. Brain circuits for the internal monitoring of movements. *Annu Rev Neurosci* 31: 317–338, 2008.
- Sperry RW. Neural basis of the spontaneous optokinetic response produced by visual inversion. *J Comp Physiol Psychol* 43: 482–489, 1950.
- Sperry RW. Neurology and the mind-brain problem. *American Scientist* 40: 291–312, 1952.
- Sterling P, and Wickelgren B. Visual receptive fields in the superior colliculus of the cat. *J Neurophysiol* 32: 1–15, 1969.
- Stryker MP, and Schiller PH. Eye and head movements evoked by electrical stimulation of monkey superior colliculus. *Exp Brain Res* 23: 103–112, 1975.
- Tanaka K, Hikosaka K, Saito H, Yukie M, Fukada Y, and Iwai E. Analysis of local and wide-field movements in the superior temporal visual areas of the macaque monkey. *J Neurosci* 6: 134–144, 1986.
- Tasaki I, Polley EH, and Orrego F. Action potentials from individual elements in cat geniculate and striate cortex. *J Neurophysiol* 17: 454–474, 1954.
- Umeno MM, and Goldberg ME. Spatial processing in the monkey frontal eye field. I. Predictive visual responses. *J Neurophysiol* 78: 1373–1383, 1997.

- von Helmholtz H. *Helmholtz's Treatise on Physiological Optics, 3rd Edition, 1910, translated by J.P.C. Southall*. New York: Optical Society of America, 1925.
- von Holst E, and Mittelstaedt H. Das Reafferenzprinzip. Wechselwirkungen zwischen Zentralnervensystem und Peripherie. *Naturwissenschaften* 37: 464–476, 1950.
- Wall PD. Repetitive discharge of neurons. *J Neurophysiol* 22: 305–320, 1959.
- Wolbarsht ML, Macnichel EF, Jr., and Wagner HG. Glass insulated platinum microelectrode. *Science* 132: 1309–1310, 1960.
- Wurtz RH. War and the living environment. *Nuclear Information* 5 (10):1–16, 1963.
- Wurtz RH. Steady potential fields during sleep and wakefulness in the cat. *Exp Neurol* 15: 274–292, 1966.
- Wurtz RH. Visual receptive fields of striate cortex neurons in awake monkeys. *Physiologist* 10: 352, 1967.
- Wurtz RH. Visual cortex neurons: response to stimuli during rapid eye movements. *Science* 162: 1148–1150, 1968.
- Wurtz RH. Comparison of effects of eye movements and stimulus movements on striate cortex neurons of the monkey. *J Neurophysiol* 32: 987–994, 1969a.
- Wurtz RH. Response of striate cortex neurons during rapid eye movements in the monkey. *J Neurophysiol* 32: 975–986, 1969b.
- Wurtz RH. Visual receptive fields of striate cortex neurons in awake monkeys. *J Neurophysiol* 32: 727–742, 1969c.
- Wurtz RH. Neuronal mechanisms of visual stability. *Vision Res* 48: 2070–2089, 2008.
- Wurtz RH, Castellucci VF, and Nusrala JM. Synaptic plasticity: the effect of the action potential in the postsynaptic neuron. *Exp Neurol* 18: 350–368, 1967.
- Wurtz RH, and Goldberg ME. Superior colliculus responses related to eye movement in awake monkeys. *Science* 171: 82–84, 1971.
- Wurtz RH, and Goldberg ME. Activity of superior colliculus in behaving monkey: III. Cells discharging before eye movements. *J Neurophysiol* 35: 575–586, 1972a.
- Wurtz RH, and Goldberg ME. Activity of superior colliculus in behaving monkey: IV. Effects of lesions on eye movements. *J Neurophysiol* 35: 587–596, 1972b.
- Wurtz RH, and Goldberg ME. The primate superior colliculus and the shift of visual attention. *Invest Ophthalmol* 11: 441–450, 1972c.
- Wurtz RH, and Goldberg ME. The role of the superior colliculus in visually-evoked eye movements. *Bibl Ophthalmol* 82: 149–158., 1972d.
- Wurtz RH, Goldberg ME, and Robinson DL. Behavioral modulation of visual responses in the monkey: stimulus selection for attention and movement. *Prog Psychobiol Physiol Psychol* 9: 43–83, 1980
- Wurtz RH, Goldberg ME, and Robinson DL. Brain mechanisms of visual attention. *Scientific Am* 246: 124–135, 1982.
- Wurtz RH, and Mohler CW. Enhancement of visual responses in monkey striate cortex and frontal eye fields. *J Neurophysiol* 39: 766–772, 1976a.
- Wurtz RH, and Mohler CW. Organization of monkey superior colliculus: enhanced visual response of superficial layer cells. *J Neurophysiol* 39: 745–765, 1976b.

- Wurtz RH, and Olds J. Amygdaloid stimulation and operant reinforcement in the rat. *J Comp Physiol Psychol* 56: 941–949, 1963.
- Wurtz RH, and Optican LM. Superior colliculus cell types and models of saccade generation. *Curr Opin Neurobiol* 4: 857–861, 1994.
- Wurtz RH, Sommer MA, Pare M, and Ferraina S. Signal transformations from cerebral cortex to superior colliculus for the generation of saccades. *Vision Res* 41: 3399–3412, 2001.
- Zeki SM. The functional organization of projections from striate to prestriate visual cortex in the rhesus monkey. *Cold Spring Harbor Symp Quant Biol* 40: 591–600, 1975.

This page intentionally left blank

Index

- Abdullaev, Y. G., 578
Ache, B., 663
Adams, D. J., 168
Adams, B., 237
Adams, S., 597
Adrian, R. H., 157, 298, 499, 511, 661, 662
Aghajanian, G. K., 18, 19, 20
Agmon, A., 263, 264
Agnew, W. S., 155
Agopyan, N., 320
Aitkin, L. M., 445
Aizawa, H., 735, 745
Akbarian, S., 269
Akil, H., 269, 680
Albano, J. E., 735, 740
Alexander, G. E., 80, 83, 84
Almers, W., 164, 178
Alonso, M., 209, 216
Andersen, P., 392, 394–96, 673
Anderson, N. C., 511
Anderson, W. W., 148
Andersson, S. A., 395
Andreose, J. S., 425
Angelakos, E. T., 649
Anisman, H., 201
Ardenghi, P., 211
Ardestani, A., 90
Armstrong, C., 512
Armstrong, C. M., 153, 166, 168, 169, 171, 512
Asanuma, C., 260
Ashford, J. W., 85
Aston-Jones, G., 37
Aungle, P. G., 287
Axelrod, J., 16, 17, 20, 21, 26, 34, 544, 681
Babcock, D. F., 179
Baddeley, A., 80, 81, 84
Baird, A. A., 130
Baker, P. F., 157
Balaban, E., 364, 367, 368
Ball, R., 177
Barnes, S., 169, 171
Barnett, R. J., 16, 17
Barros, D. A., 207, 209
Basso, M. A., 735, 740, 745
Batini, C., 369
Battenberg, E. L. F., 34
Bauer, R. H., 80
Baynes, K. B., 127, 130
Bayon, A., 36
Bekinschtein, P., 211, 215, 216, 217, 218
Belo, M., 370, 371
Benabid, A. L., 38
Ben-Ari, Y., 311, 316, 320
Bender, D. B., 728
Benson, D. L., 262
Benson, T. E., 664, 685
Berkowicz, D. A., 672, 685
Berlucchi, G., 104, 106
Berman, A. L., 260
Berman, N., 620, 633
Berman, R. A., 731, 735, 744
Bernabeu, R., 207, 208, 209
Bernstein, T., 510
Bevilaqua, L. R., 207, 209, 210, 211, 214, 215
Bezakova, G., 427
Bezanilla, F., 166
Bianchin, M., 207, 208
Billiard, J., 178
Billingham, R. E., 371
Bishop, P. O., 614, 619
Bizzi, E., 617, 618, 626, 718, 719, 722
Bjorklund, A., 544
Blakemore, C., 625, 626
Blass, E. M., 663

- Blaustein, M. P., 157, 506
 Bliss, T. V., 200, 205, 206, 208, 212, 383,
 398–402, 404–6, 414, 429–31, 432
 Bloom, F. E., 1–49
 Boch, R., 622
 Bogen, J. E., 102
 Boies, S. W., 581
 Bonini, J. S., 207, 208, 210, 211, 213
 Borges, J. L., 190–91, 196, 218
 Braddick, O., 736, 742
 Brayton, R. K., 647, 666, 667
 Breer, H., 672
 Brenner, H. R., 415, 425
 Brentani, R. R., 210
 Bressler, S. L., 89
 Brightman, M. W., 654
 Brill, M. H., 65, 73, 518
 Brioni, J. D., 200, 203
 Brito, J. M., 360
 Broide, R. S., 48
 Brooks, D. J., 549
 Brown, D. A., 175
 Brown, D. D., 254, 650
 Brugge, J. F., 445
 Bucy, P. C., 77
 Bunney, W. E., Jr., 269
 Burns, J. M., 109
 Burns, B. D., 301, 302, 398, 404
 Burton, H., 259
 Bushnell, M. C., 739

 Cahalan, M. D., 167, 170
 Cahill, L., 203
 Cajal, S. R., 60, 65, 69, 70, 190, 248,
 257, 258, 266–67, 402, 542, 651, 652,
 658, 681
 Caldwell, P. C., 160
 Calloni, G. W., 362
 Cameron-Curry, P., 362
 Cammarota, M., 207, 209, 210, 211,
 214, 215
 Campbell, D. T., 166
 Campbell, F. W., 302, 736
 Cangiano, A., 415, 416, 417, 418
 Cao, A., 632, 633
 Carnevale, N. T., 522, 667
 Carrasco, M. A., 202
 Carvey, C. E., 610, 633, 636

 Catterall, W. A., 164, 165
 Cavalheiro, E. A., 200, 201
 Cavanaugh, J., 735, 740
 Cepko, C. L., 364
 Chandler, W. K., 157, 166, 499, 500,
 522, 656
 Chang, H. C., 319, 673
 Chang, H. T., 319
 Charles, E. R., 623, 631, 634
 Charpak, S., 684
 Charrier, J. B., 366, 367
 Chaumont, F., 345
 Chaves, M. L. F., 203, 207
 Chavkin, C., 39
 Chen, W. R., 673, 674, 676, 685
 Cherubini, E., 316
 Chorover, S. L., 613, 614, 615
 Choudary, P. V., 268
 Chow, B. Y., 731
 Chu, F. C., 730
 Chu, N-s., 26
 Chun, L. L. Y., 354
 Clark, S. A., 7
 Cohen, I., 424
 Cohen, J., 37
 Cohen, L. B., 160, 656, 674
 Coitinho, A. S., 210
 Colby, C. L., 620, 623, 634
 Cole, K. S., 153, 163, 165, 489, 490, 494,
 499, 510
 Collingridge, G. L., 205, 206, 212
 Conti, F., 167, 168
 Conway, J. L., 634
 Cooley, J. W., 500, 522
 Coombs, J. S., 500, 501
 Corballis, P. M., 130
 Corbel, C., 370
 Costa, E., 14–15, 16, 22, 30
 Couly, G. F., 350, 351, 357, 358, 359,
 360, 365
 Crasto, C. J., 679, 685
 Creutzfeldt, O. D., 73, 74, 75, 620
 Creuzet, S., 350, 351, 356, 360
 Crick, F., 125, 145, 301, 614,
 653, 740
 Croisille, Y. L., 342
 Crossley, P. H., 365
 Cruzblanca, H., 176

- Dainty, J., 287
 Dale, A. M., 295
 Dalkara, T., 320, 321
 Darrow, B., 670, 686
 Davidson, R. M., 728
 Davison, A. P., 685
 DeFelipe, J., 262, 266
 Desimone, R., 626, 631
 Deyo, S. N., 35
 Diamond, I. T., 250, 253, 537, 620
 Dias, R. D., 202, 203
 Docter, R. F., 72
 Dodge, F. A., 149
 Dodge, F. A. Jr., 150–51, 152, 498, 500,
 515, 519, 522
 Dolan, R. P., 628, 629, 634
 Doron, K. W., 130
 Dowling, J. E., 627, 628, 657
 Dreifuss, J. J., 305
 Duffy, C. J., 735, 743
 Duhamel, J.-R., 738
 Dulac, C., 362
 Dunlap, K., 176
 Dupin, E., 361, 362, 363
 Durham, L., 242, 511, 604, 606
 Dürsteler, M. R., 735, 743
 Dwyer, T. M., 168

 Eccles, J. C., 14, 25, 195, 237, 292–94,
 296, 311, 319, 391, 394, 396, 397,
 398, 401, 404, 409, 413, 500, 501,
 652–54, 657–58
 Edelman, G. M., 89, 367
 Eichelman, W., 569
 Eken, T., 421
 Elder, G. C., 42
 Eliassen, J. C., 130
 Enroth-Cugell, C., 619, 621
 Erdemli, G., 321
 Erulkar, S. D., 657, 660
 Etchevers, H. C., 351
 Ettenberg, A., 35
 Evangelista, A. M., 198
 Evarts, E. V., 33, 596, 617, 662, 719,
 720, 722, 724, 726, 729, 732

 Falkenburger, B. H., 176, 177
 Fan, J., 579

 Fehilly, C. B., 370
 Felleman, D. J., 450
 Fendrich, R., 114, 117, 130
 Ferraina, S., 735, 738
 Ferrera, V. P., 624
 Fin, C., 208
 Firestein, S. F., 669, 670, 672, 685
 Fischbach, G. D., 176, 720
 Fischer, B., 622
 Fischer, E. H., 164, 291
 Fishman, H. M., 510
 Floriano, W. B., 672
 Fontaine, J., 346, 352, 355
 Foote, S. L., 27, 34, 35, 39
 Fossella, J. A., 579
 Foxman, B. T., 130
 Frankel, W. N., 300, 544
 Frankenhaeuser, B., 149, 151, 157,
 162, 165
 Freedman, S., 315
 French, E. D., 34
 Frenkel, M., 544
 Friedman, D. P., 261
 Friess, S. L., 493
 Fuchs, A. F., 721, 729
 Fuhrman, F. A., 507
 Fulginiti, S., 198
 Fumagalli, G., 425
 Funahashi, S., 84
 Funnell, M. G., 130
 Furini, C. R., 208
 Furshpan, E. J., 147, 354
 Fuster, J., 59–93

 Gage, P. W., 512, 516
 Galindo, A., 305
 Games, D., 34, 47
 Gans, C., 357
 Garcia, D. E., 176
 Gardner, D., 680
 Gattoni, R. C., 199
 Gazzaniga, M. S., 89, 99–130, 268,
 575, 681
 Getchell, T. V., 657, 658, 668, 685
 Giarman, N. J., 19
 Gibson, J. J., 744
 Glickstein, M., 104
 Goddard, W. A., 672

- Godfraind, J. M., 307, 318
 Goldberg, J. M., 541, 542
 Goldberg, M. E., 598, 619, 725, 726,
 727, 728, 729, 731, 732, 735, 736,
 738, 739, 742
 Goldman, D. E., 494, 502, 506
 Goldman-Rakic, P. S., 84, 665
 Goldstein, M., 649
 Goldstein, A., 29
 Golshani, P., 263
 Goronowitsch, N., 355
 Gozzani, J. L., 200
 Graham, A., 362
 Grapin-Botton, A., 365
 Graziano, A., 266, 268
 Greatbatch, W., 491, 492, 509, 525
 Greenfield, A., 614, 634
 Greengard, P., 22
 Greenwood, P., 130
 Greer, C. A., 664–65, 667, 671, 675, 685
 Grethe, J. S., 650, 651, 653, 655, 672,
 683, 684
 Grillner, S., 683
 Grosmaître, X., 671, 685
 Gruart, A., 211
 Guillemin, R., 29, 31, 33
 Guitton, D., 744
 Guy, N., 369

 Haberly, L. B., 657, 659, 685
 Haenny, P. E., 631, 632, 634
 Hafed, Z. M., 745
 Halasz, N., 686
 Hallonet, M. E., 364
 Hamill, O. P., 173
 Hammond, W. S., 353, 356
 Handy, T. C., 130
 Hansen, A. J., 686
 Harris, E. M., 496, 497, 504, 513
 Hartline, H. K., 149, 152, 626
 Harvey, J. A., 542, 543
 Hashikawa, T., 267
 Hayashi, J. H., 298, 304, 521
 Hayek, F. A., 89
 Heath, C. J., 255, 256, 258
 Hebb, C. O., 295, 297
 Hebb, D. O., 89, 295, 402–4, 456, 711,
 712, 713

 Hedlund, B., 669, 670, 685
 Heller, A., 542, 543, 544
 Helm, J. P., 4
 Hendry, S. H. C., 261, 262, 263
 Hennig, R., 421, 422
 Henriksen, S. J., 28, 34, 38, 39
 Henry, J. L., 310
 Herlitze, S., 176
 Herrington, J., 178, 179
 Herz, A., 75
 Hettleman, K. R., 605, 608
 Hikosaka, O., 622, 731, 735, 741, 742
 Hilgemann, D. W., 177
 Hille, B., 141–183
 Hillyard, S. A., 122
 Hines, M. L., 519, 520, 521, 522, 523,
 673, 679
 Hirai, T., 261, 263
 Hirdes, W., 176
 Hirst, W., 122
 His, W., 351
 Hochachka, P. L., 318
 Hodgkin, A. L., 7, 146, 153, 155, 157,
 158, 159–60, 161, 163, 165, 166, 167,
 168, 287, 309, 488, 494, 497, 499,
 500, 508, 510, 652, 656, 720
 Hoffer, B. J., 24
 Hokfelt, T., 26, 544
 Holt, E. B., 725
 Holtzman, J. D., 116, 130
 Honda, C. N., 263
 Hondeghem, L. M., 170
 Horowitz, L. F., 176
 Hörstadius, S., 351, 355
 Houssaint, E., 348, 349
 Hubel, D. H., 71, 83, 244, 388, 389, 442,
 457, 568, 594, 612, 614, 617, 619,
 620, 625, 627, 632, 662, 715, 716,
 717, 720, 721, 722, 723–725
 Hunt, H. F., 542
 Huntley, G. W., 263
 Huntsman, M. M., 263
 Hutsler, J. J., 130
 Huxley, A. F., 7, 70, 146, 153, 155,
 158, 159, 161, 163, 166, 170, 286,
 287, 309, 488, 497, 499, 500, 502,
 652, 720
 Hyder, F., 675

- Iversen, L. L., 20, 26, 28, 33, 35, 38
 Iversen, S. D., 20, 33, 38
 Izquierdo, I., 189–219
- Jacobsen, C. F., 79, 80, 83
 James, W., 212
 Jansen, J. K., 406
 Jasper, H., 71, 251, 260, 297,
 302, 388
 Jastreboff, P. J., 644, 664, 686
 Jeffery, W. R., 357
 Jenkins, W. M., 462, 463
 Jensen, J. B., 176, 177
 Jensen, R. V., 193
 Jerusalinsky, D., 207, 208
 Jerve, J. P., 85, 86
 Jia, C. P., 674, 685
 Jirikowski, G. F., 40
 Johnston, M. C., 356
 Jones, E., 233–270
 Joshi, D., 686
 Jouandet, M. L., 130
 Joyner, R. W., 513, 514, 515, 518
 Judge, S. J., 729, 730, 735, 737
 Julian, F. J., 70, 494, 502, 506
 Julien, J. P., 322
 Jung, J., 343
 Jung, S. R., 180
- Kaas, J. H., 449, 450
 Kaftan, E. J., 179
 Kalhovde, J. M., 420
 Kandel, E. R., 195, 209, 401,
 496, 667, 683, 720
 Kanwisher, N. G., 146, 626
 Kao, C. Y., 507
 Karapas, F., 544
 Karten, H. J., 269
 Katche, C., 217, 218
 Kato, K., 304
 Katz, B., 26, 151, 291–92, 301, 402,
 412–13, 493, 498, 500, 507, 652,
 656, 661
 Katzung, B. G., 170
 Kauer, J. S., 657, 662, 664, 665,
 668, 674
 Kawamura, H., 307
 Keele, S. W., 568, 571
- Keller, E. L., 740
 Kelly, J. S., 305
 Keynes, R. D., 160, 161, 168
 Kilpatrick, R., 287
 Kingstone, A., 130
 Kinutani, M., 369, 370
 Kirby, M. L., 359
 Kitzes, L., 445
 Klüver, H., 77
 Knapp, A. G., 628, 630, 633
 Koch, K. W., 87
 Koda, L. Y., 34, 35
 Koerner, F., 619, 633
 Koh, D. S., 176, 179
 Komatsu, H., 735, 743
 Koob, G. F., 33, 34, 39, 42
 Koppenhöfer, E., 169
 Kosslyn, S. M., 123, 569, 681
 Krauzlis, R. J., 735, 740, 745, 746
 Krieger, N. R., 193
 Križ, J. M., 322
 Krnjević, K., 279–323
 Kupfer, D. J., 20
- Lahav, R., 363
 Lai, C., 40
 Lamour, Y., 309, 320
 Lancet, D., 664, 669, 685
 Landis, D. M. D., 664
 Landis, S. C., 26, 28, 354
 Lashley, K. S., 102, 456, 576, 595,
 596, 597
 Laska, M., 678, 686
 Laughlin, S. B., 118
 Le Douarin, N. M., 335–373
 Le Lièvre, C. S., 346, 350, 351, 352,
 355, 356, 357
 Leblond, J., 317, 321
 Lecoin, L., 363
 LeDoux, J. E., 77, 108, 118, 130
 Lee, K., 631
 Lee, K. M., 737
 Leggio, M. G., 267
 Leinders-Zufall, T., 670, 671, 685
 Lerner, R. A., 38
 Levi de Stein, M., 207
 Liang, F., 263
 Lima, R. H., 39, 210

- Linden, L., 210
 Lindgren, C. A., 521
 Ling, N., 33
 Lisiewicz, A., 309
 Liu, X. B., 263
 Liu, N., 680, 685
 Lledo, P.-M., 684
 Llinás, R. R., 266
 Loeb, G., 452
 Logothetis, D. E., 175
 Logothetis, N. K., 623, 631–32, 633, 634
 Lømo, T., 383–432
 Loughlin, S. E., 35
 Lovejoy, L. P., 740
 Luck, S. J., 116
 Lutz, T., 345
 Lux, H. D., 75
 Lynch, G., 125, 401, 402
- Macchi, G., 261
 MacDonald, J. F., 309
 Maciejewski-Lenoir, D., 40
 Mackie, K., 176
 MacKinnon, R., 166
 Malpeli, J., 620, 623, 624, 634
 Mancini, R. E., 192
 Manger, P. R., 265
 Mangun, G. R., 130
 Mao, B., 685
 Marchetti, C., 176
 Marengo, L. N., 685
 Marichich, E. S., 197
 Martin, C., 370
 Martin, J. M., 463, 678
 Martinez, S., 365
 Martins, V. R., 210
 Martone, M. E., 680
 Masukawa, L. M., 669, 685
 Masurkar, A. V., 685
 Mathiesen, I., 425, 426
 Matin, E., 736
 Maunsell, J. H. R., 87, 622–24, 628, 631, 632, 634
 May, P. R., 81–82
 Mazzarello, P., 684
 McAlonan, K., 735, 740
 McCandliss, B. D., 578
 McClintock, T. S., 675
- McCormick, D. L., 266
 McGaugh, J. H., 35, 203
 McGaugh, J. L., 197, 200, 202, 203, 204, 206, 215, 216, 217, 567
 McGinty, J. F., 39
 McGonnell, I. M., 362
 McNaughton, L. A., 402, 404
 McPeck, R. M., 634
 Medawar, P., 653
 Medina, J. H., 203, 204, 205, 206, 207, 208, 209, 211, 212, 215, 217, 219
 Mehlen, P., 367
 Merlo, A. B., 196
 Meryman, H. T., 492
 Merzenich, M. M., 439–468
 Mesulam, M.-M., 89
 Metcalfe, J., 128
 Meves, H., 157, 162, 166
 Migliore, M., 676, 686
 Mikami, A., 735, 742
 Miledi, R., 293, 294, 301, 400, 408, 412–13, 507
 Mirsky, J. S., 679, 685
 Mishkin, M., 722
 Mitchell, J. F., 296
 Mitchell, R. F., 567
 Mittelstaedt, H., 737
 Mohler, C. W., 735, 739
 Molinari, M., 267
 Mombaerts, P., 661, 671
 Mommaerts, W., 156
 Moore, J. W., 477–525
 Moore, R. Y., 35, 531–551
 Morales, M., 40, 493
 Moran, J., 631
 Morris, M. E., 305, 311, 313
 Morrison, J. H., 36, 39, 47
 Morse, T. M., 680, 685
 Mountcastle, V. B., 244, 250, 253, 442–44, 446, 455, 575, 625, 650, 652–53, 716
 Mozell, M. M., 665
 Mozhayeva, G. N., 171, 182
 Mueller, D., 215
 Muller, J. R., 740
 Munoz, D. P., 735, 739, 744, 745
 Murray, K. D., 268
 Myskiw, J. C., 211

- Nakahara, H., 735, 745
 Nakamura, R. K., 108, 364, 669
 Naquet, R., 201, 368, 369
 Narahashi, T., 153, 505, 506, 507, 516, 522
 Nasello, A. G., 197, 198
 Nass, R. D., 114
 Nataf, V., 363
 Nathanson, N. M., 165, 174
 Naumov, A. P., 171, 178, 179, 182
 Nave, K.-A., 40
 Nawroth, J. C., 685
 Nelson, R. J., 450
 Netto, C. A., 203, 207
 Neumcke, B., 167
 Neville, H. J., 36
 Newsome, W. T., 735, 740, 742, 743
 Nguyen, T. T., 179
 Nicholson, J. L., 42
 Nicoll, R. A., 23, 176, 401, 660
 Nistri, A., 309
 Njå, A., 430
 Noda, M., 174
 Noma, A., 174, 318
 Nonner, W., 151, 152, 162, 167
 Northcutt, R. G., 357
 Nowycky, M. C., 660, 685
 Nudo, R. J., 456
 Numa, S., 37

 Ohkubo, Y., 360
 Ojima, H., 267
 Olson, L., 259
 Optican, L. M., 730, 732, 734, 746
 Orsingher, O. A., 197, 198
 Östman, R., 193
 Ottoson, D., 655, 656, 668

 Paratcha, G., 208, 210
 Pare, M., 735, 738
 Park, Y. B., 179
 Parker, C. W., 25
 Patterson, P. H., 354
 Paul, R. L., 445–46, 447
 Pavlov, I. P., 214
 Pearse, A. E. G., 355
 Petersen, S. E., 122
 Peterson, B. E., 462, 685

 Pettigrew, J. D., 724
 Phelps, E. A., 128
 Phillips, C. C., 650, 651, 652, 653, 654, 673
 Phillis, J. W., 296, 299, 300
 Pickel, V. M., 26
 Platt, J. B., 355
 Plum, F., 114
 Pongracz, F., 685
 Pons, T. P., 265
 Port, N. L., 745
 Porter, R., 261
 Posley, K. A., 87
 Posner, J. B., 114, 564, 569
 Posner, M. I., 122, 563–81, 681
 Pourquié, O., 357
 Prado de Carvalho, L., 200
 Prado, V. F., 211
 Premack, D., 107
 Puil, E., 309
 Pumain, R., 307, 320
 Purpura, D. P., 25
 Putnam, M. C., 130

 Quaia, C., 745, 746
 Quevedo, J., 207, 209
 Quillfeldt, J. A., 207
 Quintana, J., 84, 87
 Quirk, G. J., 215

 Rachid, C., 200
 Raichle, M. E., 122, 563, 576, 577, 580
 Rakic, P., 665
 Rall, W., 395, 643, 653, 667, 682, 683
 Ralston, E., 657
 Ramon, F., 514, 515
 Randi, M., 300
 Rausell, E., 264, 265
 Rayport, M., 119
 Real, C., 363
 Recanzone, G. H., 459, 735
 Redwine, J. M., 48
 Reese, T. S., 654
 Reiffenstein, R. J., 307, 313
 Reilly, J. F., 48
 Reinhardt, W., 311
 Renaud, L., 307
 Rescorla, R. A., 200

- Restrepo, D., 675
 Reuter, H., 157
 Reuter-Lorenz, P. A., 130
 Ricci, G. F., 388
 Richmond, B. J., 144, 730, 733, 735, 737
 Richter, R. B., 538, 539, 540, 633, 685
 Riley, J. N., 4, 5
 Rimer, M., 424, 426
 Rinzel, J., 666, 683
 Risse, G. L., 114, 130
 Rizzolatti, G., 107, 728, 740
 Robson, J. G., 303, 619, 621, 736
 Roche, J. P., 176
 Rogers, M., 569
 Rogers, J., 36
 Ropert, N., 312, 320
 Rosenkilde, C. E., 84
 Rosenthal, J., 408, 410, 414
 Roser, M. E., 130
 Rossato, J. I., 207, 209, 210, 211, 215, 216, 217, 218
 Roth, R. H., 19
 Roth, L. J., 542
 Rothbart, M. K., 578, 580
 Rothman, D. L., 675
 Roy, J. P., 735, 744
 Rubinstein, J. L. R., 43
 Rueda, M. R., 580

 Sakmann, B., 408, 415, 522
 Salaün, J., 372
 Salmoiraghi, G. C., 12, 16, 22, 23, 24, 29
 Sanna, P. P., 40
 Saxen, L., 348
 Schatzmann, H. J., 157
 Schein, S. J., 620, 623, 633
 Scheuer, T., 164
 Schiller, P. H., 585–636, 729
 Schindler, R. A., 452
 Schmitt, F. O., 18, 33, 34, 35, 46, 367
 Schreyer, D. J., 260
 Schulman, J. A., 539
 Schultze, M., 607
 Schutz, R. A., 200
 Schwark, H. D., 263
 Schwartz, F., 601
 Schwartz, S., 304, 305
 Scott, W. R., 506
 Segal, D. S., 33
 Segal, M., 26
 Segev, I., 667, 683
 Seitz, N., 157
 Shallice, T., 212
 Shapiro, B. I., 170, 511
 Shapiro, M. S., 176, 177
 Sharp, F. R., 662
 Shaw, T. I., 158, 507
 Shen, G. Y., 673, 674, 676
 Shepherd, G. M., 643–686
 Shepherd-Barr, K., 682
 Sherk, H., 626, 634
 Shindy, W. W., 87, 88
 Shoemaker, W. J., 33, 34, 35
 Sidtis, J. J., 127, 130
 Sierra, G., 76, 77, 80, 194
 Sierra-Marcuño, G., 76
 Siggins, G. R., 24–26, 28, 34, 39
 Sigworth, F. J., 151
 Simpson, J. I., 630
 Singer, M. S., 125, 672, 685, 686
 Skorpen, J., 423
 Slater, C. R., 423, 432
 Slaughter, M. M., 628
 Slipczuk, L., 209, 211
 Slocum, W. M., 633, 634
 Smirnakis, S. M., 634
 Smylie, C. S., 127
 Snyder, S. H., 29
 Soejima, M., 174
 Solomon, R. L., 200
 Sommer, M. A., 634, 731, 735, 738, 744
 Sommer, T., 579
 Sonenberg, N., 323
 Sperry, R. W., 101, 102, 103, 104, 105, 129, 620
 Squire, L. R., 91, 206, 213, 217, 373, 478, 574, 618, 633, 634, 681, 706
 Steriade, M., 266, 312, 313
 Sterling, P., 727
 Sternberg, P. W., 567
 Stewart, W. B., 657, 663, 664, 665, 685
 Stockbridge, N., 520
 Straschill, M., 75
 Straughan, D. W., 300

- Strichartz, G. R., 169
 Strowbridge, B. W., 685
 Stryker, M. P., 618, 619, 620, 625, 626,
 628, 633, 634, 635, 729
 Stuart, A. E., 515, 518, 669, 670, 671
 Suh, B. C., 176, 177
 Sur, M., 450, 626
 Sutcliffe, J. G., 38, 40, 47
 Swartz, B. E., 90
 Szabo, G., 175
 Szapiro, G., 214, 215
- Takata, M., 507, 510, 511
 Tanaka, K., 267, 744
 Tang, Y. Y., 580
 Tasaki, I., 147, 167, 166, 499, 720, 726,
 732, 735
 Taylor, R., 502, 503, 569
 Tehovnik, E. J., 621, 632, 633, 634
 Teicher, M. H., 663
 Teillet, M. A., 346, 350, 352, 353, 354,
 364, 367, 368, 369
 Tekkök, S. B. 321
 Terlau, H., 154
 Thach, W. T., 260
 Thibert, C., 367
 Thompson, R., 458
 Tighilet, B., 263
 Toivonen, S., 348
 Toliás, A. S., 631, 634
 Tramo, M. J., 130
 Trembleau, A., 40
 Trentin, A., 362
 Trombley, P. Q., 672, 685
 True, S. D., 619, 624, 634
 Tse, A., 178
 Tse, F. W., 178
 Turk, D. J., 130
- Ulbricht, W., 162, 510
 Umeno, M. M., 738
 Uyeda, A. A., 68, 69, 76, 77
- Valentino, K. L., 260
 Van Horn, J. D., 130
 Van Sluyters, R. C., 626
 Vásquez, B. J., 195, 196, 197, 202
 Vassalli, A., 671
- Velletri Glass, A., 108, 113
 Verduzco-Flores, S., 90
 Vianna, M. R., 207, 213, 214, 215
 Villa, A. E. P., 90
 Vincenzi, F. F., 157
 Viola, H., 209
 Vogel, W., 102, 162, 169
 Volpe, B. T., 114, 116, 130
 von Helmholtz, H., 737
 von Holst, E., 737
- Waldow, U., 685
 Wall, P. D., 649, 656, 724
 Walsh, C., 364
 Walz, R., 207, 209
 Wang, X., 462
 Warren, R. A., 263
 Warrington, E. R., 212
 Wassle, H., 629
 Watanabe, Y., 83
 Watkins, W. B., 299
 Waxman, S. G., 518
 Wedner, H. J., 25
 Werblin, F. S., 627, 628, 657, 669
 Werman, R., 304, 309
 Werner, H., 162, 510, 609, 611
 Wessinger, C. M., 114, 117, 130
 Westerfield, M., 498, 500, 501, 516, 522
 Westgaard, R. H., 405, 406, 414, 419
 Whitcomb, E. R., 493
 White, M. W., 452
 Whitlock, J. R., 211, 212
 Whittaker, V. P., 296
 Wickelgren, B., 727
 Wiener, M., 610
 Wiesel, T. N., 61, 71, 253, 520, 568,
 612, 614, 625, 627, 653, 662, 717,
 720, 723, 724
- Willhite, D. C., 676, 685
 Williamson, A., 685
 Wise, S. P., 235, 260
 Wolbarsht, M. L., 616, 723
 Wolff, E., 338–41, 344, 346, 361
 Wolfman, C., 205, 207, 209
 Wollmuth, L. P., 169, 176
 Woodhull, A. M., 167, 170
 Woolf, T. B., 667, 685
 Worden, F. G., 74

- Wu, C. C., 48
Wurtman, R. J., 544
Wurtz, R. H., 705–747
- Xia, A., 674, 685
Xiong, W., 673
- Yajeya, J., 84, 87
Yamamori, T., 354
Yang, J., 168, 686
Ye, J. H., 322
Yen, C. T., 261, 263
Yim, C. Y., 320
- Yim, G. K. W., 305
Young, W. G., 39, 41, 47
- Zeki, S. M., 631, 742
Zeng, S., 685
Zhao, Y. T., 320
Zieglgansberger, W., 34
Zigmond, M., 549
Ziller, C., 361
Zinn, C. G., 208
Zipser, D., 90
Zornetzer, S. F., 201
Zufall, F., 671