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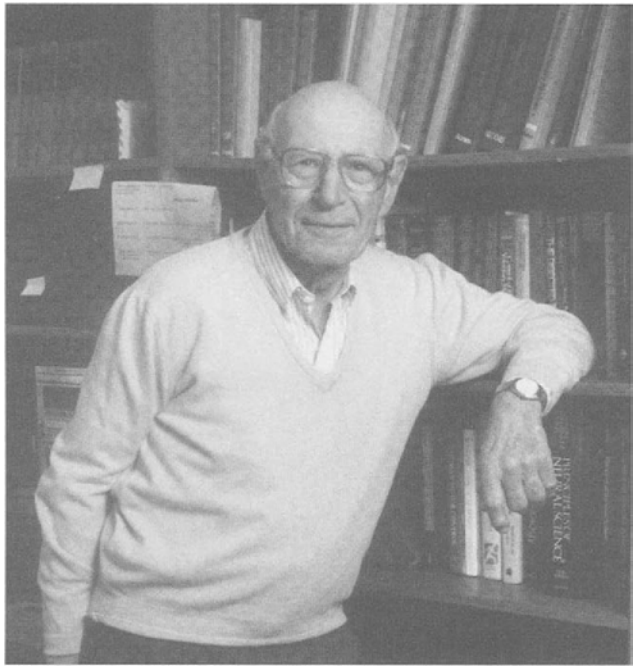

Vernon B. Brooks

BORN:

Berlin, Germany
May 10, 1923

EDUCATION:

University of Toronto, B.A. (1946)
University of Chicago, M.S. (1948)
University of Toronto, Ph.D. (1952)

APPOINTMENTS:

McGill University, Montreal (1952)
Rockefeller University, New York (1956)
New York Medical College, New York (1965)
University of Western Ontario, London, Ontario (1971)
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Vernon B. Brooks was a pioneer in studies of the neural basis of motor control. He studied the organization of motor cortex, demonstrated how the cerebellum modulates the cortical control of movement, and was among the first to study the neural basis of motor learning.

Vernon B. Brooks

Early Life

I was born in Berlin, Germany, in 1923 as Werner Bruck. My father was a lawyer in general practice and also a good pianist who played with a chamber group at our home. When I was 5 years old, my family moved from a city apartment into a comfortable suburban house. Life was tranquil, I played with the boys in the neighborhood, and my mother began to take me to museums and art galleries. She was a gentle soul who had been a painter and wrote stories for children. In the last grade of primary school, in 1933, we had a major assembly in which the form teacher explained to us what a great day it was for Germany because Adolf Hitler had been elected chancellor. After that life changed.

To my surprise I found that my playmates fell away and my parents had to explain to me that, although we had no religious life, we were considered Jews by the new government. Generations of cultural assimilation, fervent patriotism, and service as an officer in World War I (WWI) had come to mean nothing. During the next few years all manner of things changed ever more drastically for the worse, and after my father's return from Sachsenhausen in November or December 1938, my mother managed to get me on a Kindertransport to Britain where I arrived in January 1939. By that time, I had begun to wonder whether anything was left that had any meaning. For this narrative I now leave the subsequent nightmare in Germany and continue with only my story.

A new life began with a wonderful family in Kent that took me in and I started to learn how to be a farmer. I became reasonably happy in that pursuit, but it was not to last. In May 1940, when the invasion was expected, all German nationals were interned and I found myself classified as a 'friendly enemy alien,' whatever that might be, and was shipped off to the Isle of Man. By June France fell, and soon we were convoyed to Canada where internment continued, but we were considered ordinary enemy aliens because the British had not advised the Canadians who we were. It took months before this was sorted out, helped by letters from our most unusual campmate, the youngest grandson of the former Kaiser, who had been at Cambridge at the outbreak of war. The whole crazy story about our camps was described later by a former internee (Koch, 1980, 1985).

Life settled into a pretty dull routine of chores and work parties, but before too long those of us who still had to finish high school attracted the attention of some professional men who made up a school of sorts. It was a good try but it did not work because we had neither a curriculum nor any supplies. Later that year, however, a small miracle occurred through the efforts of a few enlightened Canadians, of which boys of my age knew nothing. Some supplies arrived to help us prepare for the preliminary exams of McGill University because our camp had been designated as an 'external examination center.' Many years later we learned that the camp commandant, a former prisoner of war in WWI and father of two boys of our age, had taken an active hand in helping to make that happen. The key ingredient on our side of the wire was an uncommonly qualified 'faculty' led by an extraordinary young scholar who became our headmaster. From then on we had a marvelous school of about a dozen pupils, who became friends, and as many teachers. We passed our first exams in 1941. Far more important, however, was that for most of us the meaning of values was being restored.

Sometimes I look at the picture that was taken of us pupils and teachers and marvel at the extraordinary men who taught us. The headmaster's father had been a pacifist deputy in the first (Weimar) parliament after WWI, the history teacher was a great-grandson of Bismarck, the Latin teachers were a civil servant and an order priest, mathematics was taught by a sea captain and a professional school teacher, physics was taught by two Cambridge graduate students, and so on. The headmaster led us to appreciate Shakespeare and other literature while, almost as counterpoint, we obtained an understanding of RealPolitik and multinational wars from the history teacher (who taught us the prescribed period from the end of the Hundred Year War to the beginning of WWI). It was real education and perhaps it is not a coincidence that most of us became academics, clerics, etc. Our backgrounds were as varied as those of the teachers: There were very few whose families continued to live reasonably in Germany or Austria throughout the war, while for most others their families had fled or had not managed to do so.

After that year some of the teachers were released with the help of a committee of concerned and influential persons in Ottawa, which precipitated us into our first experience of independent study for the next, university admitting, grade. I was released in May 1942 (by Order-in-Council of the Governor General as arranged by the Ottawa committee) into the care of a sponsor in Toronto and managed to pass the Ontario University entrance exams a month later. What was I going to study? As a teenager I had imagined myself as an architect, but I was advised that it would be a poor bet for me in Toronto. I had always been interested in animals, and the time on the farm in England had drawn me into scientific agriculture. Biology as a subject had been reinforced in the camp through some talks

given by Johannes Holtfreter, a famous embryologist. That fall I became a University of Toronto freshman in the honors science program, an introductory course for future scientists that kept us pretty busy. It was a bit of a breathless time for me anyway because there had been little opportunity to find out about the city, the country, or anything else. Fortunately, I lived in residence at my college (Victoria) and by the end of that year I had settled in, made some friends, and passed my exams. Since no one could pronounce my first name properly, I took a near equivalent and became Vernon. That made me feel more comfortable. For the next 3 years I studied biology because it still attracted me more than a newer course offered in 'Physiology and Biochemistry.' After university graduation in 1946, I was allowed to immigrate officially, become a naturalized Canadian citizen, and legally change my name. My family name Bruck was, painful to my ears, pronounced by most to rhyme with truck, and I chose Brooks. Now Vernon Brooks continues this report.

University Education and Beginning of Research

I nearly became a marine biologist as an upper-year undergraduate because the fisheries people eyed me as a candidate. Some Toronto zoology professors ran federal lab stations in the Maritime Provinces. The borderline between academic Toronto and the Fisheries Research Board of Canada was fluid (no pun intended). When they offered me a summer job in an Acadian French village in New Brunswick, I jumped at it. This was the best possible job—enough to clear $500, which was the sum needed for the year's stay at my college residence. I held a scholarship for my fees and earned spending money by running the residence tuck shop in the evenings. For my summer job, I worked on the culture of Malpeque Bay oysters, which were well-known but too expensive because of old-fashioned random gathering with oyster rakes on the unseen rocky bottom.

My task was to remedy this by implementing a recent zoology Ph.D. thesis on how marine larvae grow. Growth curves for the larvae had been established for different water temperatures and salinity, from which one could predict to the nearest tide when they would become too heavy to swim and would attach themselves on the bottom. The economic opportunity for the fishermen was the following: If one knew the settling tide ahead of time, then one could catch the oysters on submerged, anchored bundles of concrete-coated cardboard. This concentrated crop could then be reared in floating trays. I was to make the daily water measurements, construct the oyster larvae growth curves from plankton tows, and instruct the fishermen what to do and when. It all worked out fine, they had their first good crops and I had a great time, but I came to realize that I would not like to spend my life on this sort of project.

In my final year in 1946, during a course on comparative neuroanatomy given by E. Horne Craigie, I realized that what I really wanted to do was to study brain function. Since I was not prepared for neurophysiology and because there was little of it locally unless one first obtained an M.D., Craigie wrote me a recommendation to Ralph Gerard in the physiology department at the University of Chicago. I gratefully accepted a fellowship to take courses and have a first go at research.

Chicago

Gerard's lab was interested mainly in the metabolism of neural tissue. Great work was being done on muscle fiber membranes by Gilbert Ling, who had perfected making microelectrodes, and on nerve conduction and respiration by Bob Doty, who had developed a special microrespirometer. Stephen Kuffler was a senior fellow working on neuromuscular transmission. I was assigned, with Bob Ransmeier, to study the effects of metabolic intermediates on the electrical activity and respiration of the isolated frog brain, a preparation that Ben Libet, then still in the department, had worked with for several years. Among the welter of results there was a surprise: Fumarate could sometimes convulse the brain at a thousand times weaker concentration than other intermediates, but we could do little with this finding because there was no good rationale in 19'47 and 1948. (In retrospect, it might have related to fumarate letting more glutamate into the cells, but the transmitter action of glutamate was not discovered until 10 years later.)

While we were slugging away on this we found another attraction: Warren McCulloch, the presiding genius at the Neuropsychiatric Center of the University of Illinois, welcomed students from other universities to his fascinating seminar talks (reproduced later in *Embodiments of Mind*). His approach, through brain systems rather than chemistry, convinced me that this sort of study would surely lead to understanding how we think, and that a good way to that end might be to study how the brain governs voluntary movements. I had no grasp of psychology but knew that body language expresses emotions and attitudes and also that handwriting reflects some personal traits. I realized that a bridge was needed to link such loose phenomena to the spinal reflexes. Favorite topics have changed, of course, and today gene and brain chemistry reign supreme. An unexpected invitation resolved my indecision regarding which path to take in Chicago. Donald Solandt, professor of biophysics in Toronto, wrote to ask whether I would like to return to Toronto to do a Ph.D. in his department. I accepted the offer because I knew of his lab from a previous occasion when I had helped him create an exhibit on denervated muscle for the First International Conference of the Poliomyelitis Foundation held in New York City.

Toronto, Again

Biophysics in Toronto was a subdeptartment of physiology. I decided to follow up on Kuffler's recent neuromuscular work by comparing the effects of extra- and intracellular microapplications of the transmitter acetylcholine (ACh) to an endplate. Toward this end, I extruded ACh from a glass micropipette with pressure from a small syringe onto a thin muscle in a dish in which one could see the neuromuscular endplates with a dissection microscope. That brave-new-world experiment was vitiated, however, by ACh leakage from the pipette. (Microejection of ACh did become successful a year or two later through the use of electrical currents to control leakage, a method published by Nastuk in 1953). Continuation of my study was not resolved because Don Solandt had an illness that by 1949 and 1950 handicapped him sufficiently to cause the department head, Charles Best, to effect my transfer from Toronto to physiology at McGill University. There, Hank MacIntosh had just begun to assemble a strong group of neurophysiologists. At that time I became engaged to Nancy Fraser and we were married in Toronto before moving to Montreal.

McGill University

At McGill I continued work on neuromuscular transmission and received the delayed Toronto degree in 1952. Arnold Burgen had suggested that I continue his studies on botulinum toxin in which he had shown that the toxin shuts off the outflow of acetylcholine. My Ph.D. problem was to define this action at the neuromuscular junction. This research went well because I could show that the toxin shuts down the nerve endings before the impulse reaches the transmittter release site rather than acting on transmitter release as such. Therefore, I had a neat result that this new assistant professor noticed, to his joy, was included in Perry's report in *Nature* about interesting papers from the 23rd International Congress of Physiology held in Montreal in 1953.[1]

Hank MacIntosh created serious respect for research in the physiology department. We were in a rather decrepit building and had little research money and very low salaries, but everyone's spirits were high. Scientific

[1] Later I discovered that I had been an inadvertent godfather for the 'Botox' treatment of many dystonias and other involuntary muscle movements. In a symposium book, Therapy with Botulinum Toxin, Edward Schantz reported that 'the possible use of toxins for weakening a muscle was first suggested to me by Dr. Vernon Brooks, a physiologist to whom I furnished toxin for his studies. He had shown that the toxin blocked acetylcholine release to the muscle and he suggested in the 1950s that the toxin would be good to reduce the activity of hyperactive muscle.' This suggestion, based on my work and that of Arnold Burgen and of Arthur Guyton before me, was passed on by Schantz to Alan Scott, who used the toxin on monkeys' overactive eye muscles and, after Federal Drug Administration (FDA) clearance, on human volunteers. That batch of toxin was licensed by the FDA in 1989 and is now packaged by Allergan Pharmaceuticals as Botox.

conversation flourished, for me mostly with Ben Burns, with whose family Nancy and I shared a house on a farm outside of Montreal. We also shared cars and on the way into town we usually talked science; these talks were great tutorials. Hank made sure that students and faculty alike got a chance to meet with the greats who came to visit. I remember meeting Edith Bülbring, Steve Kuffler, and Ragnar Granit. I particularly remember an evening with Alan Hodgkin sitting on Hank's living room floor with us, the young crowd, and challenging us to invent new techniques for tackling the nervous system, and then discussing our inventions with us.

'Neuro,' as we called it, was a staggering growth industry at McGill in the early to mid–1950s. Physiology buzzed with never-ending talk. Don Hebb, professor of psychology, had already published his book *Organization of Behavior*, Peter Milner and Jim Olds were discovering the 'reward' centers, and we could watch Jasper working with Penfield from the glass-enclosed balcony over the operating room at the Montreal Neurological Institute (MNI) while Brenda Milner talked to the patient under the drape tent. During that period, the reticular nuclei were mapped by Jerzy Olszewski, the transmitter action of GABA in the mammalian brain was discovered in Allan Elliott's lab, and Herbert Jasper directed great laboratory research in the MNI fellowship program. The names of Jean Pierre Cordeau, Yves Lamarre, David Ingvar, Cho-Lu Li, and Alan Rothballer come to mind from that time, and of course David Hubel, who was learning electroencephalography. All the conventional disciplines were in play; I suppose their local talk and seminars were creating 'neuroscience' but that name did not surface until 20 years later. During the Montreal period, a pied piper came to town to give a lecture—John Eccles. He had already begun work on spinal reflexes that would earn him the Nobel prize 10 years later. Listening to that man made me want to work with him, and fortunately he supported my wish to come to the newly formed Australian National University.

Canberra

In 1954 my family and I went to Australia by ship, I as a fellow of the Medical Committee of the National Research Council of Canada, forerunner of today's Medical Research Council of Canada (MRC). My main experiment was to follow up Sherrington's suspicion that tetanus toxin interfered with 'central inhibition'; this we confirmed by showing that the toxin depresses spinal reflex inhibition through interference with transmission near inhibitory synaptic junctions.

The physiology department at the Australian National University was a small, but very exciting, place because Eccles maintained an unremitting drive to understand the mechanisms of spinal integration. The department was really his laboratory group that consisted of Jack Eccles, his daughter Rose, Jack Coombs, Paul Fatt, Bill Liley, David Curtis, and myself. I was

teamed up with David Curtis, and we worked well together. Eccles spent his mornings writing, and then joined the experiment after lunch and worked with us until it was done. The John Curtin School was still a building site and we worked in army-style prefabs. The campus was unfinished and Canberra in general was in transition. The master plan for the city had not yet been implemented, and the site of the planned central lake was still sheep paddocks, but University House, just finished at the shore of the future lake, had come complete with a vice chancellor's barge that sat on the grass. Housing was scarce because the Public Service was being moved into town from Melbourne; but the university had managed to reserve housing for personnel such as us. When we arrived Landgren was just about to leave, and since Koketsu had just left, we were moved into the vacated flat.

Eccles used to pick me up first thing in the morning and drop me off usually in time for a late supper or even later at night after a long run. The experiments were lengthy because we obtained as many inhibitory curves of various reflexes as possible, in addition to intracellular recordings from spinal motoneurons. The longest experiment ran for 3 days, by which time it taxed the air-conditioning. The first evening of this run, Eccles and I, with our wives, were dinner guests of the Canadian High Commissioner. We left David to carry on and went home to dress for dinner (black tie, of course). At the end of the evening Jack thought it would be jolly to drop by and see how David was doing. We found him rather fatigued but the cat's reflexes were so good that he carried on alone through the night until morning; then Jack and I returned and worked through that day, and David came back later! That experiment confirmed everything we had already seen in bits and pieces and yielded a letter to *Nature*.

Life in Canberra was always laced with great promise and it was never leisurely. For instance, after the first 3 months Eccles thought that I did not have enough to do and suggested that I should extend my extracellular botulinum toxin studies done at McGill by having Paul Fatt and Bill Liley show me how to do this with intracellular recording. (At that point David Curtis and I were already doing two spinal cord cats a week, always with complete data analysis before the next one; at home we had a 3-year-old, Nancy was pregnant with our second child, we had no car, and we had no respite—so why not add a day of neuromuscular work and its analysis? Well, yes, of course!) I got a setup going with the help of Paul and Bill and Jerry Winsbury, the chief technician. Soon I was able to pinpoint botulinum toxin block to the very tips of the nerve terminals from which acetylcholine is released.

A question left on the table from that study was, What guards the transmitter content of nerve endings, and specifically how far could transmitter release be potentiated by repetitive nerve stimulation? The amount of ACh available for release at the neuromuscular junction is backed up by a

reserve store that is at least 1000 times as large. I addressed what prevents it from depletion under normal conditions later with Roger Thies at Rockefeller in 1957. We found that mobilization of the ACh reserve is slow and that the ACh content of nerve endings is preserved because the amount of transmitter released by each nerve impulse becomes smaller as nerve stimulation frequency is increased, and also because during very intense neural bombardment nerve branches stop conducting altogether.

When we began our homeward voyage to Canada a year after our arrival in Australia, I was elated about what I had learned, but we were exhausted. On the overwhelming plus side, however, I have long since realized that I had acquired a mind-set that would carry me along for decades.

Arrangement of Topics from Now On

Factual material about all aspects of this memoir and some photographs can be found on my web site at: http://publish.uwo.ca/~brooks/.

Research

Up to this point the narrative has been chronological. From here on, however, it seems more useful to describe my investigative work as a simple flow of research topics. Each topic will be described as an entity, although several times they were carried over from one institution to another and, inevitably, the topics overlapped. The topics are, broadly, (i) organization of motor cortex, (ii) cerebellar modulation of the cortical control of movements and postures, and (ii) motor learning.

Organization of motor cortex began at Rockefeller in 1956 and was completed after I had moved to the New York Medical College (NYMC) in 1963. This is where the work on cerebellar modulation of motor cortex began in 1968, but it was continued at the University of Western Ontario from 1971 to 1979. Motor learning had its origin in the work on motor cortex and on cerebellum by the very nature of cortical programming and of cerebellar control. From 1961 on, learning was mentioned in or generated sections in papers or separate, small publications. It became a major topic in publications dating from 1983 to the present.

A Word about Citations and the Lively People in the Lab

After an initial period of working alone I was fortunate to have been associated with many fine coworkers who helped greatly in shaping our productivity. It is not possible to list all their contributions, but coworkers' names appear in the following account and in their selected contributions in Some Relevant Papers from the Lab in the bibliography; they are also cited in the listed 'reviews.' The motor cortex is discussed in Brooks and Stoney (1971) and Brooks (1981), the cerebellum is discussed in Brooks and Thach (1981),

the reversible lesions by the cooling method are discussed in Brooks (1983), movement programs are discussed in Brooks (1979, 1985), movement adaptations are discussed in Brooks (1984), and limbic contributions to motor learning are discussed in Brooks (1986b, 1990).

Teaching and Other Matters

Teaching, major writing projects, convening special meetings, and institutional appointments are important but they not necessarily related to research areas. Therefore, they are grouped together at the end just before 'A look back' that closes my account.

Organization of Motor Cortex

The Rockefeller Institute

After Montreal and Canberra, I was led to New York in 1956. This came about because, at the 1954 federation meetings in Atlantic City, a few months before we went to Australia, David Lloyd had invited me to join his laboratory (department) at the Rockefeller Institute after our return, which I gladly accepted. Later I discerned the connection: Eccles had been David's supervisor in Sherrington's Oxford lab. David expected his younger colleagues to follow their bent and not to depend on him. I resolved to study the cerebral control of voluntary movements since I had held the (rather vague) view since Chicago days that if we could penetrate the underlying planning in the brain it would probably reveal something about how we think. In 1955 and 1956, during a final teaching period at McGill, I made a plan for recording from single cells in motor cortex as a next step up from the spinal cord. To this end, I elected to study the natural inputs to pyramidal tract (PT) cells and their peripheral receptive fields and also to search for 'antidromic' inhibition of PT cells through intracortical axon collaterals of their neighbors, analogous to spinal Renshaw inhibition.

The period beginning in 1955 was one of important discoveries about the sensory and motor cortex, notably by Vernon Mountcastle and Charles Phillips, with both of whom I had begun to correspond before moving to New York. In 1955 Mountcastle's first notes had appeared about peripheral receptive fields of neurons in radially oriented columns in cat's primary sensory cortex, and he was about to submit the papers of which he had sent me manuscript copies. This work convinced me to check out the equivalent story in motor cortex. Also in 1955, Phillips had produced the first evidence that antidromically activated PT cells could depress spontaneous firing of nearby PT cells. I resolved to apply such tests to PT cell responses to natural peripheral stimulation. Phillips wrote me in 1955,

> As one who was once an undergraduate pupil of Jack Eccles, I like to feel that we are all members of a happy scientific

> family! The easiest way for me to answer your questions about what has already been done is to send you these spare proofs of papers.

Jack, as one came to know him once one had left his lab, was such a charismatic teacher/leader that many of us bonded with him and with others, sometimes for life, in the way he described in his letter to me.

Some introductory remarks are in order about Rockefeller, as we called it, or the Institute. It was a wonderful place even before the campus of today came into existence. The library and all support services were superb and run in a gentlemanly fashion that generated a family feeling between faculty and staff as well as the collegial attitude among the scientists, old and young. The paneled library in Founders Hall was above the grand lunchroom, whose windows overlooked the East River. Lunch was a hot one-course meal that was served on long, linen-covered, set tables, and we signed a chit for the modest charge. One was expected to sit in any empty place, introduce oneself, and converse. Some tables were livelier than others, but none were ever dull because one never knew whom one might meet. I remember one occasion when I met a German visitor who had been sent by the Max Planck Society to see how our transformation into a university was working out because the society was searching for a way to rejuvenate its institutes in which all faculty still had lifetime appointments. After we had introduced ourselves we discovered common interests: He was Richard Jung, the foremost German neurologist and neurological researcher. Later, he invited me to his institute in Freiburg, where I met his associates, and colleagues in other universities, who occasionally sent coworkers to my lab.

Neurophysiology was housed in Theobald Smith Hall, where Herbert Gasser, the former director, worked in his lab at the end of the first floor. The rest of that floor was occupied by David Lloyd on one side and Lorente de Nó on the other. Keffer Hartline and Frank Brink housed their groups on the upper floors. For those who were running long experiments, Gasser had had a small cafeteria installed in the basement where good scientific talk could be had during an evening's supper break. If the experiment ran too late to get home, the basement also offered a room with a shower unit and some spartan cubicles with beds.

Construction of elegant low-rise buildings began around the time of my arrival. Caspary Auditorium, known familiarly as the dome, came into being. It is a superb piece of architecture, with a beautiful auditorium and wonderful acoustics in which, besides lectures, regular concerts were held. A new administration and social center stretched in front of Theobald Smith and Flexner Halls, and to the south a student residence was built. The opening of the university was marked, in 1957 I think, with a 3-day celebration that featured a ball, concerts, ceremonies, lectures and talks of

various kinds, and tours of the newly landscaped grounds. Nancy and I enjoyed it all, and no one was left in doubt that we were set on a most serious road to high purpose. The high-rise towers for labs and for residences began to sprout in earnest only later.

A word about research support is in order because it is a constant worry for today's scientists. During my first year or two at Rockefeller, outside support was frowned upon despite the new extramural National Institutes of Health (NIH) programs. This changed gradually: I remember the first tentative, apologetic approach from the business manager suggesting that I might consider requesting partial support for animal charges. Within fairly short order we all acquired regular grants, of course, but they never involved salaries.

First Attack on the Motor Cortex

On arrival in 1956, I assembled gear for working with the cat's motor cortex in the lab vacated by Cuy Hunt in Lloyd's laboratory. I began with exposed brains protected by an oil pool, but vascular pulsations made even extracellular PT cell recording too hazardous for quantitative exploration. Nevertheless, exciting differences from primary sensory cortex did become apparent right away even with open brains and with immobile animals. PT cells often had convergent inputs from diverse adequate stimuli such as hair bending, touch, pressure, and joint movements, and their peripheral receptive fields could be small or much larger, even encompassing several limbs. Repeated testing with sensory stimuli could make responses of PT cells 'labile' so that they became responsive to new influences and from larger fields. Interactions between converging sensory inputs and surround inhibition were easily demonstrated. PT cell peripheral receptive fields clearly had subliminal fringes that in some ways resembled those of spinal motoneurons. Responses of PT cells to sensory activation were inhibited when the medullary pyramids were backfired. The motor cortex had begun to show me how it was set up as a coordinating device! I soon discovered that my findings were not unique: Harry Patton and Arne Towe in Seattle were also studying PT –cells, although with slightly different methods, and during the next few years we enjoyed a happy fellowship in comparing data.

A Look Ahead

Let's look ahead to the payoff that came from these first solo efforts. They led my lab to descriptions of how convergent somatosensory inputs are organized in radially oriented cortical input columns in motor cortex and of effects from active PT cell axon collaterals on naturally evoked activity of neighboring cells. The results implied that collateral, recurrent mechanisms could fine-tune the pyramidal output to the spinal cord, and do so as efficiently as spinal recurrent inhibition. The recurrent effects on

neighboring cells included extrapyramidal ones, for instance, corticorubral neurons, in a way that creates a balance control for cerebral and cerebellar influences on the spinal cord. By 1966, work with animal 'acute preparations' would become too limited in scope and I would begin studies of cerebellar influences on the motor cortex with task-related behavior of monkeys.

Help from the Eye of a Living Fossil

While I was obtaining first results with the motor cortex in 1956 and 1957, an exciting new functional meaning for recurrent interactions between neighboring cells appeared. Floyd Ratliffe reported in a faculty seminar about the work he was doing with Keffer Hartline on cellular responses in the compound eye of the horseshoe crab *Limulus* (work that led to the Nobel prize 10 years later). Ratliffe described how visual contrast between two illuminated points in that eye is reinforced by inhibition exerted from one light receiving ommatidium onto the neighboring ones through axon collaterals. It was an overwhelming experience to learn about these results with a sensory system because the story sounded very much like the Renshaw inhibition in the spinal motor system that I had learned about in Canberra only a year previously! Sharpening of borderline contrast now seemed a likely functional purpose for the Renshaw story which still lacked a convincing teleology. Possibly, recurrent inhibition could assist in refining muscular control by sharpening the accuracy of spinal reflexes, and do so by improving their focus on their target motor nuclei. Such 'motor' contrast between adjacent nuclei would be a good tool in adjusting movements.

Recurrent Inhibition Focuses the aim of Spinal Reflexes

I could hardly wait to do the equivalent experiment of Hartline and Ratliffe's visual story with cat's spinal reflexes to determine if backfiring of motoneuron axons would produce motor contrast. The means were to hand because stretch reflexes respond to repetitive excitation by activating not only their target nucleus but also nearby 'off-target' motor nuclei that act in concert with it. Since Renshaw inhibition operates through axon collateral branches of spinal motoneurons by means of acetylcholine (ACh) synapses, one should be able to depress these off-target fringe components with anticholinergic drugs. I talked to my colleague Victor Wilson about the idea right away but said that I did not know how to evoke monosynaptic reflexes fast enough to be inhibited by the rapidly repeating recurrent volleys. Fortunately, he had learned how that could be done from Mike Fuortes at Walter Reed. (Threshold stimulation of the nerve to one head of a muscle at rates that would normally produce sustained contractions elicits 'on-target' reflexes in the stimulated nerve as well as off-target reflexes in the nerve to the other head of the muscle. The motor nuclei of

the two heads are located next to each other.) Therefore, Victor and I worked together with gusto and dispatch, the essential results about recurrent inhibition depressing off-target reflexes more than on-target ones accumulated quickly, and we could state that recurrent inhibition can prevent spread of reflex responses. In other words, it sharpens motor contrast. We submitted a note that fall and a full paper the next year. What a romp!

How Natural Sensory Stimulation Can Drive Neurons in Precentral Motor Cortex

My initial findings on sensory inputs to motor cortex were quantified with Pablo Rudomin, who began working with me in 1959. Together with Clifford Slayman, we accumulated a sample of over 200 cells that gave a first hint about their input–output relations. It was known that information about natural stimulation of a given part of the body was relayed to cortical neurons that, according to then known motor maps, influenced spinal output to muscles in that body part. It was only a hint since we did not demonstrate this for our cells, but we did note possible integrative arrangements. For instance, skin and hair input to a limb depend on limb position and might thus coordinate interaction of inputs between limbs to support movements. Such neurons were intermixed in the cortex with others that responded to deep pressure and joint movement. The spread of labile receptive fields, described in my early solo efforts, transcended the usual neurophysiological microsecond order of time by two or three orders of magnitude. Such a time course was also that of habituation, which suggested that labile field spread might reflect mechanisms that could be active during attention, such as reticular input and even higher control levels, which could also be used for learning. By the same token, the properties of wide fields made me think of possible inputs from the thalamic anterolateral and unspecific systems. It was a stretch to extend our data to what might happen in the natural state, but in a few years we would break out of that chrysalis.

Once more, it was reassuring to find ourselves not alone. Vernon Mountcastle told me in 1960 about recent work of Pierre Buser, who had shown maps of 'global' fields for cats' PT cells. He had indeed obtained similar results to ours and, moreover, at the same time, but his first notes had been published only in French and so had escaped my attention. Also, his first English presentation was in Rosenblith's symposium on sensory integration, held in 1959 in Boston, that I had not known about at the time. I compared our main illustrations in 1961 in Hernández Peón's Mexico symposium, 'The Physiological Basis of Mental Activity,' at which I also reiterated the possible connection to arousal, attention, and learning. Further comparisons of our data to those of Buser and of the Seattle group were made in Purpura's meeting on the 'Neurophysiological basis of

normal and abnormal motor activities' held in 1966 and once more in a chapter in *Annual Review of Physiology* (Brooks and Stoney, 1971).

Radial Columns of Precentral Cells Are Activated by Diverse Modalities But with Overlapping Topography

The peripheral input story reached its goal in 1964 and 1965 when we defined radial columns in precentral motor cortex by the common somatic, 'topographic,' locations of their peripheral inputs with Carol Welt, Jürgen Aschoff, and Kazuo Kameda. The results were clear: Three-fourths of our new sample of over 200 neurons within radially aligned columns had overlapping topography, but they received a mixture of inputs from skin, deep receptors, and joints. Neurons with fixed local inputs provided the radially oriented, somatotopic framework that also accommodated the foci of the other one-fourth of neurons, including those with large 'wide' receptive fields. These columns, defined by overlap of their receptive fields, had diameters of up to 0.4 mm. (They were established by histological reconstruction of cell locations in the microelectrode tracks and by the distance across the radial orientation without significant changes of local receptive field locations. This method had become feasible because we now prevented vascular pulsations by using closed chambers over the exposed brain.)

The most conspicuous feature of the sensory input to the primary motor cortex was the convergence of various sensory modalities into a more or less somatotopic arrangement, in contrast to the primary sensory cortex in which all cells in radial columns receive common topographic and modality-specific inputs (Mountcastle, 1957). These were indications of motor cortex function as a coordinative device, in contrast to the discriminative function of the somatosensory cortex. Of course, functions and control systems for behavior were difficult to discern from data obtained with immobile animals. However, we knew, of course, that the motor cortex is an executor rather than an initiator because 'decisions' to move, or even how to move, were apparently made elsewhere to be passed on to the corticofugal systems for processing (Paillard, 1960; Eccles, 1967). My experimental approach changed after Purpura's meeting in 1966 when I saw the power of recording single, task-related PT cells in monkeys that were behaviorally active under controlled conditions (Evarts, 1967). I realized that we had passed a watershed and decided to adapt the new method to tackle modulation of motor cortex function by the cerebellum.

Before discussing our study of cortical recurrent inhibition that followed the columnar input story, I need to give completion to this aspect of motor cortex function by discussing Hiroshi Asanuma's later work on motor cortex input–output relations. After our original collaboration at Rockefeller in 1961 and 1962 on recurrent effects, Hiroshi returned from Japan in 1964 and 1965 to join me at NYMC. It is worth mentioning one of the bonus academic experiences at Rockefeller—the president's visitors.

Dr. Bronk had his old neurophysiology friends visit and spend time with the young people in their labs, which was great for us and probably gave him useful feedback. At one of Granit's visits, in 1961 when Asanuma was in the lab with us, we talked about my sensory input story to motor cortex and also about the recurrent effects that Hiroshi and I were studying. Granit urged that the spinal outflow of the PT cells should be established. I was not too keen on that line, but perhaps Asanuma had paid attention because fortunately he did just that the next year after returning to Japan. He and Hideo Sakata facilitated reflex activity in muscles from particular radially aligned arrays of PT cells by local microstimulation through the recording microelectrode. Since the effect depended on the intact corticospinal tract, they could demonstrate that a spinal motoneuron pool is activated by colonies of closely spaced PT cells that project to that pool. It was exciting for Hiroshi and me to juxtapose our results in an illustration for Purpura's meeting in 1966.

At NYMC, Asanuma and coworkers went on to demonstrate that each efferent zone in radial columns of primary motor cortex receives inputs mainly from a skin region that is likely to be excited further during movement when the target muscle contracts. In other words, skin input reaches cortical motor columns predominantly from regions that lie in the pathway of limb movements. When Asanuma and I showed these results to our colleague Alan Rothballer, Alan exclaimed how strongly this positive feedback reminded him of Bard's 'placing reactions.' Thus, it came to be described as possibly serving the tactile placing reactions that help to position the limbs accurately in standing and walking. We all took pleasure in learning from one another. In reviewing this development of inputs and outputs of columns serving mostly one muscle, I stressed that tight preferential input–output coupling reveals only minimal building blocks from which natural cortical function could be synthesized. After all, radial arrays of cortical cells with common spinal targets were defined by local intracortical stimulation, but normal somatic input reaches many such arrays. While individual columns can be focusing devices for single muscles, only collectively and under higher control can the distributed system integrate execution of movements.

The positive input–output feedback discovered by Asanuma and coworkers could also serve other 'cortical reflexes' such as the 'instinctive tactile grasping reactions' that form part of simple exploratory movements (Denny-Brown, 1960). For instance, when a moving target is being handled, the cortical muscle drive generated by skin contact can function as a tracking system that tends to cause the limb to follow the source of stimulation and keep it on target. Asanuma's group expanded these studies and we had a good collegial relationship while my group began to study cerebrocerebellar interactions by means of local cooling of cerebellar output nuclei.

Accuracy of Motor Cortex Output Is Enhanced by Cortical Recurrent Inhibition

My original efforts regarding cortical recurrent inhibition received systematic examination when Hiroshi Asanuma first joined me at Rockefeller in 1961, as mentioned previously. Our aim was to demonstrate a cortical equivalent of the motor focusing produced by spinal Renshaw inhibition described previously. This was indeed revealed by the inhibitory trimming of the edges of peripheral receptive fields of PT cells (edge stimulation always evokes weaker responses than the field foci). This striking result of improved focusing on the most intense sensory input, and hence on motor output, was obtained by backfiring the pyramidal tract, and it suggested that natural recurrent effects may assist in fine control of corticospinal responses to input from the body surface. Since this inhibition closely resembled that obtained after afferent inhibitory components had been minimized, it constituted the strongest evidence at that time for intracortical inhibition. (We compared inhibition obtained by pyramidal backfiring with that produced by stimulation of the chronically deafferented internal capsule.) A nice addition to the earlier spinal story was obtained with Kazuo Kameda and Bob Nagel: The efficiency with which cortical recurrent inhibition reduced PT cell responses was the same as that reported for spinal Renshaw inhibition from Granit's lab.[2]

A Cortical Balance Control of Cerebral and Cerebellar Influences on the Spinal Cord

A logical next step was to determine what influence the corticospinal pyramidal neurons had on neighboring extrapyramidal cells, for instance, corticorubrospinal cells that project to the cord through the midbrain red nucleus (RN, n. ruber). The cerebellum now enters the picture because RN receives input from the cerebellar output nucleus interpositus, which projects to the spinal cord. The experiment was made possible by the arrival of an expert on the red nucleus, Nakaakira Tsukahara, who knew from previous experience how to identify rubrospinal and RN cells. This steeped us in cerebrocerebellar interactions and, together with Derek Fuller, a clear result was obtained. We found that pyramidal collateral actions from large, phasically firing PT cells activate connections that

[2] I cannot resist a eulogy of a favorite Rube Goldberg invention of mine that made life easier before we had computers. In order to analyze lengthy inhibitory curves of unit firing in brief bins of time for statistical analysis, taped unit discharges were registered by a counter for the duration of movable sweep of a cathode ray oscilloscope. That counting sweep was moved forward bin by bin through the curve duration by a programmed mechanical camera drive. The trick was that Steve Pischinger, our Austrian master mechanic who had come with me from Rockefeller, had made an angled gear that linked that drive to the counting sweep dial to let us get printed lists of cell firing for each bin: great home-made technology!

would favor the pyramidal system for movement onset and termination (that both depend on phasic firing) but that collaterals from small, tonically firing PT cells would favor the extrapyramidal system for postural tasks (that depend on tonic firing). This story would figure in Tsukahara's later work on the role of RN in motor learning based on his discovery of plastic corticorubral synapses (Tsukahara *et al.*, 1983; see also footnote 6). Analysis of recurrent interactions had now branched out, but it had also reached its limits without seeing the circuits operating in animals that were engaged in performance of intended tasks. It was time to change methods.

Mention was previously made of Dr. Bronk's visitors with respect to Ragnar Granit. Another memorable person was Adrian. I remember talking with him in my lab when I was following up an old experiment of his about spreading cortical surface responses to electrical stimulation of the cat's suprasylvian gyrus. It was approximately 1958 when Per Enger and I found that one of those responses became reinitiated after having spread a few millimeters, which was difficult to explain even for Adrian. Sometimes experimental results need some new reference to find their explanation. In this instance, it came 20 years later when new anatomical methods recognized two functionally distinct regions in that gyrus of the cat. Our responses probably were reinitiated when they spread from one of those suprasylvian regions into the other (areas 5 and 7).

Cerebellar Modulation of the Cortical Control of Movements and Postures

How the cerebellum controls the contribution of motor cortex to voluntary movements became the active goal in 1966. The anatomy was favorable inasmuch as the cerebellum, by means of its unique side path connections, was thought to handle higher motor instructions through its input from the prefrontal cortex, in contrast to the medial part whose input comes from the periphery and the midbrain red nucleus (Eccles *et al.*, 1967). A suitable use of chronically prepared animals came together in my mind in the mid–1960s after having seen Jack Brookhart's 'standing dog' experiment in Portland and Ed Evarts' monkey apparatus at NIH (Evarts, 1967; Brookhart, 1971). It was necessary to connect physiology and anatomy with movements while the animal was performing a previously learned, measurable task. An interesting method presented itself when Seth Sharpless at Einstein, a former student of Don Hebb's, called me in 1966 to view an arrangement that he and Bob Byck were using for local cooling of the sensory thalamic nucleus VPL in mobile cats. I was shown a cat walking about on a leash with connections to the apparatus, and when the cooling probe was turned on sensory-evoked potentials in primary sensory cortex disappeared! I was most impressed with this way of creating a

temporary, reversible lesion in a behaving animal, and so a cooling machine was made for my lab that put us in the chronic monkey business by 1967[3] and ushered in the most productive period for the labs with the most significant results.

Turning Cerebellar Nuclei Off and On Again

Which task would be the most suitable for our purpose? Derek Denny-Brown had urged me to study voluntary reaching (complex, multijoint) movements directed at a target rather than (simple) movements restricted to a single joint. As it turned out, we used both kinds.

The first trials, with reaching movements, foreshadowed much of what we would find in later detailed studies, just as the initial trials with precentral unit recording had done more than 10 years earlier. We reported at a symposium of the Fulton Society held in New York in 1969 that cooling the dentate nucleus, the cerebellar output to motor and premotor cortex, reproduced the same signs of neocerebellar lesions in monkey as were known for man: an inability to control the hand in goal-directed behavior because movements failed to start and stop with the proper timing. Dentate cooling degraded reaching toward a target because the movement trajectory became inaccurate and often oscillatory at the end. Corrections thus lead to ataxia, ataxic tremor, and postural tremor while trying to hold still. We did not know exactly why this happened, but we noticed that the normally distinct sequence of agonist–antagonist EMG patterns was slurred and thus degraded the timing of sequential movements in the task sequence. A significant observation was that the changes produced by cooling depended on the difficulty of the task and on the level of the monkey's training: Normal patterns reverted toward pretraining levels during cooling. We had encountered the learning capability of the cerebellum, already envisaged by Eccles *et al.* (1969).

The experiments were performed with the monkey sitting in the chair after a cooling probe had been inserted into a chronically implanted probe sheath. Around this small animal, a large crew was at work: Fred Horvath, Adam Atkin, Derek Fuller, Inessa Kozlovskaya (an exchange scientist of the U.S. and Soviet academies), and myself. Masatake Uno briefly joined us, but his main effort came with the subsequent papers on simple, single-joint movements about the elbow (described later). The three-dimensional reaching task was abandoned in favor of a two-dimensional handle-turning task because we had no methods for recording movements in multiplane workspaces. This would change within a few years, but in the meantime we got on with what was in hand.

[3] Actually, the cooling method had surfaced earlier, in 1964, when Buser described its use in tracing afferent paths to motor cortex of immobilized cats. In discussion of his paper, I had presented our first approximation of motor cortex input columns (Buser, 1966).

The second, main trials, with simple arm movements, followed Gordon Holme's dictum that the essentials of cerebellar dysfunction are best revealed by study of simple movements. We used a self-paced step-tracking task to guide a freely moving handle alternately between two targets whose positions, in the same plane, were displayed to them on a screen. Monkeys had to hold the cursor on target for a few seconds before they were signaled to begin the return movement to their former starting point. The animals gained juice rewards for correct task performance without regard to how they achieved it.

Our reversible lesions revealed that monkeys continued to know what to do despite 'unwilling' arms (Gordon Holmes, 1939) which led them to perform less efficiently. By cooling dentate (but not by cooling interpositus, the main cerebellar output to the spinal cord), we could replicate Holmes' list of movement errors: range, rate, force, and regularity of movements. Specifically, dentate cooling led to a loss of previously learned, anticipatory control of arm movement execution when approaching the target area. This caused overshoot of the target due to prolonged arm acceleration and delayed deceleration, which led to degraded movement trajectories with overcorrections, oscillations, and irregular rhythm. We had obtained clear indications that dentate cooling undid previous learning of how to execute a task but not of knowing what to do to for rewards in the task setting. Loss of programmed movement execution during continuing task performance also became evident some years later for cooling of the inferior olive, the source of cerebellar climbing fibers that are probably learning related (Gilbert and Thach, 1977). I had found what I had dreamed about 20 years earlier in Chicago—a readable link between movements and 'thinking'! It was by no means a grammar; rather, I thought of it as a partial alphabet.

Movement Details Furnish an Entry into Motor Control

I characterized simple arm movements by their velocity profiles from the beginning in 1969. Well-learned movements were mostly made as one relatively fast step, with a single velocity peak preceded by a period of acceleration and followed by one of deceleration. I called these movements 'continuous' because they ran their course without interruptions, following Gordon Holmes' (1922) nomenclature. Slower movements lasted longer than continuous ones and had successive ('discontinuous') steps with more cocontraction. Use of continuous movements depended on the animal's degree of certainty about task conditions, which showed up over time in their training records or when their task was changed after training (or during dentate cooling). Well-trained monkeys used continuous movements consistently and managed to retain their use during cue deprivation, whereas less well-trained ones fell back on discontinuous movements that were less efficient for the job.

I explained the two movement types at every opportunity because no one else was talking about this simple link between the intent for a movement and how it is executed. My purpose was to popularize the idea that simple measurements of movement velocities could reveal whether movements were programmed or whether they depended extensively on external feedback. It seemed so important to tell our story to others! My term 'continuous' was synonymous with Bizzi's later 'bell-shaped velocity profile of movements of moderate speed.' The work was presented at several conferences in the early 1970s, by which time our lab had moved to London, Ontario.

Before the move to London, we upgraded from paper records to tape recording and installed torque motors that could oppose or assist handle movement. PT cell recording began before the move and continued in London from June 1971 onwards. We recorded cell firing when the handle loaded or unloaded the monkey's effort with steady loads.[4] David Cooke and Steve Thomas produced our first movement analyses with a PDP–12 computer that enabled us in 1973 to publish the first detailed description of the temporal structure of movements, presented previously only as excerpts from paper records. They also put together a programmable analog–digital system for the experiments that was improved later by Tutis Vilis. The new equipment was first used in association with Bob Dykes and Joëlle Adrien, who had already labored hard to make cooling intelligible with post hoc histology by establishing brain isotherms for local cooling. Their experiments, although cut short by their departure, indicated that weights opposing arm movement increased discharge rates of PT cells during movements against loads and, in equal measure, increased movement velocities. We had a glimpse of cortical load compensation. The results with steady loads were followed up later with Bastian Conrad and Mario Wiesendanger and revealed that the rate of increase of PT cell firing frequency before movements start is set beforehand; that is, it is programmed. Unexpected hindrance of the arm intensified the rate of increase of cell firing so as to accelerate compensating responses of the arm to an impeding load.

[4] The move from New York to London, Ontario, was made easy because Joëlle Adrien, and Bob Dykes with his family, as well as Steve Thomas, came to London for the summer to see the lab get started. We prepared for the move by getting all material ready and practicing disconnect–reconnect of the instrument racks. In the meantime, a monkey room and a suite of labs had been built at Western, with a second monkey setup made by Bob Kager, a German master mechanic who would continue to look after us very well. Several implanted monkeys were flown up at the end of May 1971; records and equipment followed, and we, the transition crew, congregated to live as a coop in a furnished house for a month. We made our first successful recording experiment within 3 days, which amazed us all. Ordinary life resumed in July when my family arrived and we moved into our new house.

The Cerebellum Enables Motor Cortex to Deal with Errors of Voluntary Movements

The early 1970s were a very productive period in which we built on the finding from the 1960s that reversible lesions of the cerebellar dentate nucleus degrade movements in the classical manner of cerebellar lesions. Now we could proceed to how the cerebellum modulates motor cortex control of intended movements. By this time, Phillips (1969) had proposed that transcortical reflex (long-loop) responses might assist maintenance of movements working against loads. The hunt for this elusive response was discussed at a satellite meeting in Zürich of the 25th International Congress of Physiology in 1971 by Mario Wiesendanger, who was an organizer of that meeting. He joined our department in London in 1972 and worked with us while his lab was being set up. My thought was that we had a good chance to demonstrate transcortical responses as well as their cerebellar guidance if we could study how movements are restored after a limb has been knocked out of its planned trajectory. This would put our new torque motors to good use together with our experience on dentate cooling, recording of EMGs, and cell discharge in motor cortex. The idea was made feasible after Wiesendanger introduced the use of brief torque pulses to perturb limb actions, which yielded crucially better timing of events than the steady loads used in the past. The work proceeded in successive association with him and Bastian Conrad, Kenichi Matsunami, and Justus Meyer-Lohmann. Elaboration of this topic, and of the predictive nature of cerebellar control for intended starting and stopping, followed later with Jon Hore and Tutis Vilis.

The transcortical response revealed itself for the first time amid a flurry of excitement in late summer of 1972. Brief perturbations applied to arm movements altered discharges of task-related precentral neurons so as to reduce mismatch between intended and actual movements, which we reported in the *Society of Neuroscience* in 1973. The interactions between elbow perturbations, early responses of precentral neurons, and subsequent elbow movements amounted to cortical servocontrol of rapid load compensation. This could also underlie the functional stretch reflex described by Melville Jones and Watt (1971). Normal dentate function was shown to be essential for correct execution of programmed activity because it prevents unwanted stretch reflexes from setting the limb into oscillations that make movements clumsy in the execution of the task.[5] This occurs largely because the lateral cerebellum sends a predictive signal

[5] How to beat clumsiness was the theme of the first annual Stevenson Lecture, given on 'the role of the brain in movement and skill' by Sir John Eccles at the University of Western Ontario in October 1972. I inaugurated this lecture series that commemorates my predecessor, Jim (J. A. F.) Stevenson, who died unexpectedly in Zürich in the preceding summer when we were attending the 25th International Congress of Physiology.

to the precentral motor cortex to maintain as well as to start and stop movements before reflex oscillations can occur.

Phillips' postulated cortical long-loop response was the second of two successive precentral cell responses to brief torque pulses. There was a brief 'early' cortical response to the torque-imposed, passive limb displacement that was followed by several 'late' responses. All were coupled to corrective movement changes. Our significant contribution to this exciting story was that dentate cooling selectively degraded only the first of the late cortical responses and the corresponding movement corrections. We were scooped from being the first to publish about cortical reflexes as such (due to delayed publication of our work: Ed Evarts had preceded us in 1973 and 1974), but we published our results anyway, of course, together with the unique description of the cerebellar, corrective contribution (Meyer-Lohmann *et al.*, 1975). Despite the delay, our satisfactory results made us all happy in the end.

I had asked Mario to let his name stand on all papers with torque pulses because he had introduced them, but he refused because he wanted to start his own new lab. His name therefore appears for the first time in a shorter piece on load compensation and its dependence on cerebellar support. That paper had a particularly fine illustration (Conrad *et al.*, 1974; in Massion's CNRS symposium in Aix-en-Provence) that shows cortical reprogramming to restore the original, intended trajectory after an arm perturbation. It was reproduced in Kandel, Schwartz, and Jessel's third edition of *Principles of Neural Science*. We just simply had a great result, which justified the technical difficulties of the cooling method. Its arcane plumbing and troublesome controls would soon give way, in the hands of others, to new ways of producing reversible lesions, but it had served us well. I continued to think of long-loop responses as an essential tool of the brain for running motor programs of intended movement, as distinct from the goal setting for intended actions (Brooks, 1979, 1985). This was a further homecoming to my old idea of espying intent in the execution of movements.

The story of the late precentral cortical responses became even better in 1974 when it received a second reading after Jon Hore and Tutis Vilis had joined the group. They established a good working relation with Justus Meyer-Lohmann, who was back for another visit. Together, they noticed that the late cortical response during load compensation actually began with a separate, and different, component. We could report, as before, that cerebellar cooling left the early response unchanged but could add that cooling specifically diminished the newly discovered second precentral response (which previously had been disguised as the leading edge of the first of the late responses). That second response, a sharp spike, accurately times the cerebellar support for cortical load compensation and thus preserves the learned 'set' by predictive reprogramming of perturbed movements.

Routes for Cerebellar Influences in Movement Programming

An important conceptual guide about cerebrocerebellar communication was the seminal review by Gary Allen and Nakaakira Tsukahara (1974). Their scheme for support of movement programming by a cortico-cerebello-cortical circuit resonated in the writings of many of us. Following their thinking, we portrayed our second precentral response as likely resulting from relay of the early precentral response to the cerebellum, then back to cortex again from cerebellum via the dentate or interpositus nucleus. The point of preemptive, predictive cerebellar intervention was argued from the latency of normal cortical and muscular responses and from their changes during cerebellar cooling. This line of thought about cortico-cerebello-cortical circuits was developed further by Vilis and Hore (1980) in relating late precentral response oscillations to terminal cerebellar tremor after loss of cerebellar phase advance for agonists and antagonists. It is this phase advance that normally enables set. The argument was applied particularly to the predictively early, stop signal for braking of antagonist muscles to preadjust against expected perturbations (Hore and Vilis, 1984).

Tutis Vilis had led the story on set and predictive braking, whereas Jon Hore took the lead in explicit demonstration of the cerebellar mechanism for delayed onset of voluntary movements, a basic cerebellar movement disorder cited by Gordon Holmes. Jon initiated a study with Justus of a simple reaction time (RT) task in which we found that the cerebellum participates in generation of prompt arm movements most likely by transmission of a phasic movement instruction to motor cortex. The basic evidence was that dentate cooling increased RTs for both EMG and movement onset without uncoupling the discharge timing of most precentral neurons from movement onset; that is, the tight coupling from the cortex onward was maintained. The delay was caused by the loss of early, predictive, cerebellar start signals (Meyer-Lohmann *et al.*, 1977).

Sometimes We Ask an Inadequate Question

The most likely route from cerebellum to cerebrum for instructions to start and stop movements seemed to be the ventral lateral (VL) thalamic nucleus. Alan Miller and I examined the effects of cooling VL on limb perturbations with the expectation that this would interfere with compensation of set-dependent items such as reaction time and the EMG ('M2') response thought to result from long-loop action. Alan worked hard on this with well-trained monkeys but no interference could be found. The problem defied us in 1978 and 1979 because we tested monkeys only after they had learned the task, whereas Pierre Buser at that time, unbeknownst to us, had found that VL was important for task execution only while

learning the task and not thereafter.[6] His work with cats performing a visually guided reaching task was described in 1979 in a Warsaw colloqium (Fabre and Buser, 1980). Our initial results were described in the United States in 1980, with papers following thereafter; it was a hard lesson.

The Inferior Olive Supports Learning Much Like the Lateral Cerebellum

While the VL work was in progress, Hans-Georg Ross, Phil Kennedy, and I began a study of the effects of olivary (IO) cooling because the complex spikes of cerebellar Purkinje cells evoked by IO activity were thought to be related to motor learning (Gilbert and Thach, 1977) and thus probably also to learned motor programs. Again, we worked on well-trained monkeys, but in this case we obtained a useful result. We found that optimal neocerebellar control of arm movements indeed depends on climbing fiber projections from the inferior olive since cooling its principal nucleus depressed discharge of complex spikes and was accompanied by regression of movements to their prelearning state. Movement oscillations resembled those seen during dentate cooling. A significant result was that cooling IO, just as cooling dentate, degraded how movements were executed without, however, degrading the animals' knowledge of what they had to do to gain fruit juice rewards. The experiment was made possible by a clever method for inserting a cooling probe into the flexible brain stem that was designed by Kennedy and Ross. A soft plastic guide tube, implanted under X-ray guidance, could safely accommodate the stiff metal cryoprobe once the monkey's head was held steady.

A Short Foray into the Basal Ganglia

In the mid–1970s, the function of the basal ganglia was an enigma, in part because lesions in animals had not reliably reproduced the motor disorders known to occur in man. Perhaps local cooling would prove to be a useful technique? A brief trial with Jon Hore and Justus Meyer-Lohmann

[6] The findings by Fabre and Buser and by Miller and Brooks were reconciled by Ito (1984) on the basis of a model reference system, a long way from where we were in 1979 and 1980. Ito reminds us that VL projects to interpositus as well as dentate and speculates that during motor learning, motor commands are switched from cortico-corticospinal to cortico-rubrospinal lines. He posits that before learning, a cerebral attention mechanism engages fast-conducting corticospinal tract cells. That favors cerebral over cerebellar control because signals from fast PT cells inhibit slowly conducting corticorubral cells and rubrospinal tract cells (Tsukahara *et al.*, 1968). With practice, ever more precise intended movements are thought to be generated by modified action of the cerebellar side path on fast-conducting corticospinal cells. At the same time, the slowly conducting corticorubrospinal pathway would learn the model of the skill (through its plastic synapses, having been taught by VL). During task execution after repeated practice, the attention mechanism would shut down, and with it also the previously facilitated cortico-corticospinal pathway, leaving the slowly conducting cortico-rubrospinal pathway to implement the learned skill.

showed that cooling in the output region (globus pallidus) produced a severe breakdown in the performance of the step-tracking task when monkeys had no visual information about arm position, but not as long as such information was displayed to them. Jon and Tutis pursued the story further with an EMG study in 19'78 and 1979, particularly with a view to defining the movement deficit. They found that task failure was caused by incorrect balance between agonist and antagonist muscles needed for moving and holding appropriately in task context.

Trials with Human Subjects

While this work was going on, David Cooke (1980) related the timing in human subjects between late reflex EMG responses to arm perturbations and the compensation to restore the intended movement trajectory. In this work, and in his other work, he used a human-sized setup that consisted of a handle and a torque motor mounted next to a barber chair. David established quantitative relations between agonist and antagonist muscle discharges in instructed movements of human subjects (Brown and Cooke, 1981). The first human studies from the lab group (with the cooperation of neurologist John Brown) also showed that elbow movements made by patients with Parkinson's disease depended more on visual guidance than do those of normal subjects. Vision helped patients overcome an arm flexion drift, particularly when the required direction of effort was made unpredictable (Thomas *et al.*, 1977; Cooke *et al.*, 1978). The lab is referred to at that time as a lab group because I had persuaded the MRC to establish program project grants of the sort that I had negotiated with NIH before transferring the lab to Canada almost 10 years earlier. We were proud of our grant number, PG1, but when our individual projects matured in different directions it became preferable to carry them on separately.

Motor Learning: Determining What to Do and How to Execute It

Monkeys

I began to think about learning in the 1950s when I first encountered labile peripheral fields, which made me consider their possible relation to habituation, attention, and alerting mechanisms and thus perhaps to adaptation and learning. These issues came to the fore years later when I saw that cooling the dentate nucleus slurred previously learned, and precise, relations of muscle activity to successive phases of arm reaching movements. This degraded EMG precision due to inaccurate timing was confirmed quantitatively with simple arm movements in a move-and-hold step-tracking task, as discussed previously. The theme that skilled

movement execution is acquired during task learning runs through our early reports and papers (Brooks *et al.*, 1961; Brooks, 1963), as does the idea that skill learning, but not task learning, is reversed by dentate dysfunction (Brooks, 1985).

I was considering learning early because I inspected and kept the paper records of movements in the training sessions for the monkeys. The kinematic movement details were the giveaway to skill learning. The step-tracking task required the monkeys to move the handle into the target and to hold it there for a specified length of time that was signaled to the animal by auditory and visual cues. The monkeys could move any way they wanted (including when they wanted to begin), but their fruit juice rewards depended on observing the imposed time limitations. At first, they made directional and holding errors, but gradually they learned what was required of them to gain more rewards. This was reflected in their achieving task performance at better than at chance level, at which time they began making many (continuous) movements with single-peaked velocity profiles. We called this the beginning of 'insightful behavior.'

Monkeys Learn 'What' before Learning 'How'

It had been my constant theme since first describing continuous movements in 1970 that how those movements are executed demonstrates that they had been programmed. This seemed clear because accelerations and decelerations were learned together as a matched set; that is, they were matched predictively, including the use of premovement inhibition. I finally decided to publish our simple lesson that learning what to do precedes learning how to do it. As described previously for monkeys' simple elbow movements, correct performance of 'how' increases consistently only after correct 'what' has passed the chance level.

To put numbers on this statement we compared the required, appropriate, task performance and the use of programmed movement execution. (Task performance was called 'appropriate' if the target was reached without errors of direction and, in addition, if the handle was held within the target until the next trial). The learning curves began with uncertainty about the correct way to execute the task. The combined data of four monkeys yielded two intersecting straight lines relating use of continuous movements with progressive behavioral skill ('motor skill in task context'). At the intersect near 50% of behavioral skill (i.e., at the beginning of insightful behavior), the second straight line rose upward toward certainty, plotting the linearly increasing use of continuous movements. The learning data were plotted by Sherry Watts from a prodigious number of measurements for all trials in all training sessions of four monkeys (Brooks *et al.*, 1983; Brooks and Watts, 1983, 1988; Brooks, 1990). We immediately found confirmation about self-selection of accurately

programmed movements while monkeys' learned a task similar to ours in Steve Wise's lab (Weinrich *et al.*, 1984).

An interesting incidental observation concerned movement 'adaptations,' changes that are not carried over from one session to the next (Ito, 1984). We noted that velocities of continuous movements changed during training sessions but were not remembered at the next session. Late in motor learning, however, when the animals approached their best performance proficiencies, velocity adaptations were finally incorporated into remembered movement programs although the animals were not rewarded for these adaptive changes. Incorporation into memory was swift; it took only 50–100 movements once it had begun (Brooks, 1984), which is the order of magnitude for monkeys learning to correct perturbed wrist movements (Gilbert and Thach, 1977).

Movement Reaction Times Become a Rosetta Stone

Our kinematic story about learning gained a very useful link to neurophysiology with Kazuo Sasaki's presentation in 1983 at a meeting for Eccles' 80th birthday held in Göttingen, Germany. Sasaki, like us, had followed his monkeys' progress during training. His learning curves for performing a single-joint wrist movement showed, just like ours for elbow movements, an upward break at the beginning of insightful behavior, as indicated in his data by a growing preponderance of short visuomotor RTs to cues for trial start. I returned home to examine our RTs, and sure enough, our four monkeys' RTs shortened much the same way when they had passed the beginning of insightful behavior as judged by their use of continuous movements.

The equivalent shortening of RTs in the two kinds of experiments enabled us to relate our records of movement details, 'kinematics,' to Sasaki's records of cortical activity. His RT shortening coincided with a switch from cortical potentials in association cortex to those in premotor cortex, indicating cerebrocerebellar communication. (RTs were shortened by about the same length of time as they were lengthened during cerebellar cooling, reported by us in 1977.) Also, the appearance of his cerebrocerebellar potentials coincided with our increasing use of continuous movements (which fits with their progressive disappearance during dentate cooling). Furthermore, the disappearance of potentials from association cortex at the time of behavioral insight is in accord with the proposal that initial trial-and-error learning of a task, before behavioral insight, involves representational memory operating through prefrontal projections to parietal and premotor cortical areas (Goldman-Rakic, 1987). I compared Sasaki's and our results in the context of a learning hypothesis after I had visited his lab during a sabbatical in 1984 and 1985.

During that sabbatical year I formulated an idea about the role of the limbic system in motor learning that had been brewing in my mind ever

since I had joined the department in London, where Gordon Mogenson was pursuing the story of limbic connections through the nucleus accumbens. I could see that limbic actions could generate reward-related locomotion (Mogenson *et al.*, 1980), but did the limbic system have anything to do with other intended, task-related movements? In the second term of my sabbatical in New York I was at Edelman's helpful Neurosciences Institute, then located at Rockefeller. Among other things, it facilitated visits from people I wanted to learn from and talk to about my notion, which was not a current topic at the time. This stay led to the recognition of convergence between limbic and motor-related paths and a hypothesis about their action in learning (Brooks, 1986b, 1990) and also to my later studies of motor learning.

Cingulate 'Error' Potentials Point to the Limbic System

During the Göttingen meeting in 1983, a visit to Sasaki in Kyoto was agreed upon to determine how we could further exploit the commonalties in our findings. On reviewing some tapes of his monkeys' performance and cortical potentials, we found two instances in which records had been taken from the lower bank of the anterior cingulate gyrus. We looked for that site because of its possible contribution to motor learning, an idea that I had developed during the preceding months in New York as part of a sabbatical year. The cingulate records yielded a felicitous observation for trials in which the animals made inappropriately self-paced movements instead of waiting for their cue. This occurred when they had reached the halfway point of appropriate behavior as judged by their RTs. The observation was that inappropriate movements were accompanied by P3-like potentials from the anterior cingulate (but only at this stage of pivotal uncertainty and not at other times during training). We described the findings with the comment that these error potentials might reflect a cingulate activity that is related to the animals' uncertainty about stimulus relevance, and that this could lead to improved task performance. At that time cingulate cortex was thought to be entirely limbic. This story also appeared in my subsequent proposal for limbic assistance in motor learning (Brooks, 1986b, 1990).

How Does the Limbic System Assist Motor Learning?

Review of neuroanatomical and physiological data made me realize that the task-oriented premotor areas quite possibly received convergent inputs from at least two limbic system components, the cingulate cortex and the amygdala, which suggested a mechanism for their operation during motor learning. Not only might that provide confluence of cognitive and reward-related, achievement-oriented, information but also the thought occurred that such convergence might furnish a comparator for cognitive and limbic goal setting. Such a scheme could conceivably work

because the cingulate output already contains the result of another, direct input from the amygdala; that is, cingulate output to other motor-related areas would already know what the amygdala had 'told' those areas directly. Such a comparator could, in theory, set and maintain set points through corrective feedback of the relevant control systems. This proposal is hypothetical because it is extremely difficult to prove that such requisite connections in the nervous system actually do function as comparators. (A comparator, as in a thermostat, compares a desired temperature, set by a control mechanism, with the actual one and operates the furnace so as to maintain the desired temperature setting.).[7]

I was keen to encourage investigation of limbic assistance in motor learning and therefore listed some possible sites for anatomical convergence and some possible pathways that might create comparator action (Brooks, 1986b, 1990). Initially, the hypothesis attracted much attention, but it then dropped out of sight because the anatomical information was in flux and other evidence was too sparse. Happily, recent evidence for convergence of limbic and motor-related paths is accumulating for some cingulate and other cortical areas as well as for the ventral striatum. In fact, the cingulate is now emerging as a major confluence for task-related and limbic control systems by both anatomical and electrophysiological means. Details of what I had in mind will change, of course, but I enjoy following these developments.

Behavioral Insight of Human Subjects

Using the term 'behavioral insight' when monkeys go from initial task learning to acquiring skilled behavior (and skilled motor execution) was convenient but it is anthropomorphic. We cannot tell what animals are thinking, and so the time had come to ask primates who can talk. Computer games for human subjects offer an easy means to distinguish between learning 'what' and 'how.' To make subjects learn a novel rule (or strategy), I chose a task in which adoption of an unusual rule was mandatory because they had to gain control over an apparently runaway display

[7] The model for my proposal was that of Lundberg (1971) for a cerebellar comparator to maintain desired spinal actions on muscles set by supraspinal, descending control fibers. His model operates by comparing signals from primary afferent fibers (the 'room temperature') with signals from descending supraspinal control fibers (the 'desired temperature'). Comparison becomes possible because both kinds of signals are forwarded from the spinal cord to the cerebellum (ascending in the ventral spinocerebellar tract; VSCT). VSCT cells in the cord receive copies of primary afferent signals (room temperature) as well as of those from descending supraspinal control fibers (desired temperature setting). This mix of copies is obtained from certain spinal interneurons that inhibit spinal motoneurons but that also provide copies of their output to motoneurons to VSCT cells. In the simplified language used previously, VSCT output to the cerebellum therefore 'knows' what the descending control systems has told the spinal interneurons to do and also what has actually been sent to spinal motoneurons. The cerebellum is assumed to decode those signals and correct the instruction.

cursor that was, unbeknownst to them, guided by rate control (in which cursor velocity is modulated by hand position rather than hand velocity). The subjects' goal was to guide the cursor into a target. The correct motor strategy for task success with rate control is to make successive, oppositely directed hand movements by which to govern the rise and fall of cursor velocity.

We asked subjects to tell us what they were thinking while they executed the test and while we recorded their utterances, movements, and task failures and successes. Many subjects declared their insight into strategy early, after initial trial-and-error learning and before having achieved task success. This allowed us to distinguish between declarative and procedural knowledge (Squire and Zola-Morgan, 1988, 1991). Subjects' first strategy declarations stressed that the direction of hand movements had to be reversed, whereas the later declarations about suitable tactics referred to when this reversal had to be made. Those first tactical declarations required imminent or actual task success, which was achieved near asymptote on their learning curves. During their sigmoid upswing of tactical skill, use of correct timing and shaping of continuous movement tactics changed from uncertainty to certainty. We had supported our monkey studies with a clear demonstration that many human subjects can learn 'what' before learning 'how.'

The project began during a few weeks' visit in 1989 to Hans-Joachim Freund's department of neurology at the Heinrich Heine University in Düsseldorf, Germany. Frank Hilperath, a young psychologist, and I had fun exploring ways of achieving our goal (Brooks *et al.*, 1995). After my visit, Hilperath carried on to do the main work, with some oversight by Hans-Georg Ross, professor of physiology in Düsseldorf and a former coworker, on cooling the inferior olive in London. The other coauthor Brooks is my son Martin, who designed and managed the all-important final statistical evaluation of the data. This was a nice transition into mandated retirement and it came with a bonus. That paper opened the way for a functional magnetic resonance imaging study of motor learning that is ongoing in London with Ravi Menon and Francis Graydon.

Teaching and Other Matters

Teaching and Appointments

My teaching experience at McGill became useful at the Rockefeller Institute when it became a graduate university. Frank Brink, the dean, had sent a flyer to all faculty shortly after I arrived to announce that we were free to participate in teaching if we wanted to do so. When I was at McGill I most enjoyed teaching an advanced lab course in neurophysiology that I had set up for a few grad students and senior undergrads. I

responded to Brink's call by offering to prepare something along those lines, which was accepted. We had three complete setups for experiments to be done by a few students per table, ranging from the neuromuscular junction to brain. Experiments lasted all day, and students could visit at other times as well. Our key provision was that Victor Wilson and I, and later also Hiroshi Asanuma, were on hand full-time during the weekly teaching day and were also accessible on other days. There were no lectures, just the assigned reading and experiments. However, Victor and I lectured in a general introductory course for all graduate students. Once a week I also taught neurophysiology to the residents in Fred Plum's neurology department at Cornell University Medical School, located across the street.

I was offered an appointment at NYMC in 1963, probably because of my experience with organizing and teaching at McGill and at Rockefeller. The offer attracted me partly because the college had grand plans for expansion, including one to relocate from Manhattan to Westchester County. We lived in that area, about 45 minutes north of the city, and the thought of driving into a park-like setting instead of commuting to the city was appealing despite the enormous, and frightening, difference between the institutions. I joined NYMC and collected faculty for a physiology department separate from the existing joint department with pharmacology. A senior person was needed for neurophysiology, and fortunately Hiroshi Asanuma, who had gone home to Japan in 1962, let me know that he was keen to return and he came back in 1964 and 1965, as related previously in the research context. At NYMC in Manhattan we taught medical students, and some graduate instruction also began, but unfortunately the grand plan for building a Westchester campus failed at the end of the 1960s, and most of the faculty that I had recruited left on my advice.

We returned to Canada in 1971 when Ontario universities were in the periodic process of reversing the 'brain drain' to the United States, and other offers in the United States entailed leaving our much beloved home of nearly 20 years anyway. The most agreeable offer for me and Nancy came from a well-established provincial university in Ontario, the University of Western Ontario in London, that had a good medical school and associated health science departments. The department of physiology welcomed me as the new chairman in 1971, but after 5 years I let go of that burden to regain my capability in research. I have remained here happily, and I am now emeritus since mandated retirement in 1988.

Our International Meeting about Motor Control in 1968

Motor control had had its formal opening as a field in the Western world with a symposium, 'Muscular Afferents and Motor Control,' led by Ragnar Granit in Stockholm in 1965, followed by his book, *The Basis of Motor Control*, in 1970. In the meantime, Yahr and Purpura had us consider the

'neurophysiological basis of normal and abnormal motor activities' in 1966. After Purpura's meeting I decided to organize a satellite meeting to be held after the 24th International Congress of Physiology in Washington in 1968. It was held in Westchester County, New York, and actually became a more general meeting than its title, 'Motor Control by the Cerebrum and Cerebellum,' indicates. There was no plan to publish our proceedings. The freedom from print was both good and bad: We lost the chance to collect special papers and their discussion, but we gained a singularly informal meeting with much discussion and many exchanges of insight. Informality was furthered by the relaxing setting. My wife Nancy had scoured the county and came up with a winner: a local college in a lovely setting. We were allowed to take over the whole of Elizabeth Seton College with generous help from the Mother Superior, who was eager to assist this international gathering, particularly since it included scientists from the Eastern bloc of nations. Summaries of each session were finally written by the session chairmen, and our report yielded an unusual set of authors (Brooks *et al.*, 1970). I have always believed that the meeting was particularly successful because we were all seeking the unifying framework of motor control when we were still doing studies with particular brain systems. We were ready to fly our own flag.

Teaching and My Text about Motor Control in 1985 and 1986

The University of Western Ontario had a well-run graduate school to which, in time, we added an interdepartmental neuroscience program. The custom in physiology was that faculty could teach their own specialty as an elective one-term lecture course for fourth-year science undergrads and graduate students. I developed such a course on motor control, in which no lectures were given; rather, only assigned readings were given which we discussed around the table with no more than 12 participants. The final take-home exam usually consisted of a picture with the request to write about what happens in the brain when a person or animal in the picture engages in the task that it seemed to be planning or carrying out. Course topics gradually expanded to include motor programs and motor learning. This little course was my pleasure, particularly when graduate physical therapists with several years' practical experience began to enroll. They were shy at the beginning but always wound up leading the science students because they understood very well indeed how humans execute and learn to make movements. Their profession began to interest me, and I made a point of watching them in action with patients and also spoke to some special groups and at their large annual (APTA) gatherings.

Over the years, interaction with students in my course led me to transform its content into a textbook, *The Neural Basis of Motor Control* (Brooks, 1986a). The original suggestion for this had come years before from Anne Gentile at the Department of Movement Sciences at Columbia

University Teachers College. I finished writing the book in that department during a sabbatical year in 1984 and 1985 in New York, divided between Columbia and Rockefeller, except for a couple of months in Japan. It was fun and rewarding to discuss draft chapters with the graduate students in movement sciences, largely because most were experienced physical therapists. I was happy that my course worked as well in New York as it did in London. The evident usefulness of the published text gave me deep pleasure since my purpose in writing it had been to explain the field to a diverse audience.

The American Physiological Society Handbook Volume about Motor Control

The textbook had been preceded by a formative venture in science writing, the handbook volume on motor control. Early in 1977, Jack Brookhart had asked me to write the chapter about the cerebellum for a forthcoming volume on motor control that he was assembling for the *Handbook of Physiology* series published by the American Physiological Society (APS). I had been busy collecting my thoughts about the cerebellum for several meetings, including the 26th International Congress of Physiology in Paris. Later that year, however, Brookhart had to resign from the editorship of that volume because of sudden ill health and he asked me to take it over. I did, and I formed a partnership with Tom Thach for my own chapter for which we wrote our own parts and then cut and pasted them to each other's satisfaction. Getting the handbook together took over a year, even with a reduced teaching load. It was exhilarating to be able to shape this book—to choose the topics and the authors. The APS allowed me an open draw for telephone use that was very useful for getting informal advice, making contacts, and keeping in touch. All authors agreed to have their chapters refereed. Vernon Mountcastle, editor of the series on the nervous system, was immensely helpful throughout. We read all submitted work, exchanged our comments, and the results, amalgamated by me with the outside referee reports, went to the authors. All chapters went through some emendations and the authors, and later the readers, were pleased with the volume that was well received.

A Look Back

Development of Motor Control and of Neuroscience

In introducing *The Neural Basis of Motor Control*, I described the development of motor control as a

> heady time, when common concerns became obvious for disciplines that were soon to merge into Neuroscience.. . . Since the early fifties Granit and Eccles had led the way in studying the

> integrative action of the central nervous system by means of cellular analysis and McCulloch had propounded theoretical means to show that the brain was a computing machine made of neurons. Motor control was born in the sixties amidst a flood of new facts and rules.. . . Terms such as purpose, volition and reflex were redefined in the sixties and seventies. Engineering models began to enrich our views by assigning roles in control systems to modular assemblies of neurons in many parts of the brain. Comparisons of intended and actual occurrences became recognized as control devices. Analogies to the logic flow of computer programs became commonplace. Feedback and feed-forward controls, serial and parallel processing, and finally functions of distributed and adaptive systems, all found their neural counterparts.

The second half of the 1960s was germinal for our new niche, motor control, and by the 1970s we had settled comfortably in it. At the same time, we had also moved into neuroscience at-large. The Society for Neuroscience was founded in 1969 with less than 1000 members and held its first meeting in 1971. However, for several years in the late 1960s we—that is, about 200 persons interested in spinal cord and up—had met for a special half-day organized by Kay Frank and Mike Fuortes each year before the opening day at the federation meetings. The first volume of *Annual Review of Neuroscience* was published in 1978, the year we had a symposium for Jack Eccles titled 'Information Processing in the Nervous System' in Buffalo.

Personal Highlights

What were the scientific highlights for me? The most elating part was that I helped to create the field of neural motor control through laboratory work and conceptualization, and in addition that I had the opportunity to convene a formative conference on that topic, put together the first handbook on motor control, and wrote how I saw the story as a text for a more general audience.

With regard to particular research projects, there were perhaps four highlights that I could single out. The first was the establishment of the convergent radial input columns in motor cortex and of a mechanism for focusing cortical motor output. This set the stage for teasing out the functions of motor cortex. The next, more important one was the demonstration that the cerebellum supports motor programs through predictive assistance in starting, stopping, and maintaining intended movements and postures. This illuminates how the cerebellum assists in learning and carrying out motor skills. The third was the overarching discovery that details of simple movements can reveal the operation of motor set and

motor programs and can indicate the timing of behavioral insight during motor learning. Finally, a latter-day consequence of the third, was the finding that human subjects learn what to do before, or at the same time as, learning how to execute a motor task. These last points forge new links between motor control and psychology, with reference to declarative and procedural knowledge.

What does it all add up to? I suppose it is by such steps that neuroscience evolves. For me, it became possible by combining electrophysiology, anatomy, reversible lesions, kinematics, clinical history, and psychology. Luck, serendipity, and fine coworkers help. By producing new results, this evolution influences that of the constituent disciplines and neuroscience at-large; these are two-way roads. They are such great roads to travel!

At the beginning of the account of my research I said that it would be described as a simple flow of topics, although projects spilled over from one institution to another. Well, this is what I have done, but that introductory remark put it perhaps a bit mildly. When I return from a trip, I retain the best scenery and the good feelings about great encounters, but I never fasten on dark days when it pours or on wrong turns taken on the road. That is dull. I like to return home happy about what went right. And so it is, of course, with this trip through my life. It was a good run with worthwhile effort that gave me many moments of joy and deep satisfaction. Also, it gave me friendship with wonderful people. I am lucky in having been blessed with a supportive family, and this year Nancy and I celebrate our golden anniversary. We have had a good life; how can one ask for more?

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