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BORN:

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July 28, 1940

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University College London, B.Sc.
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APPOINTMENTS:

University of Washington, Seattle (1968)
Medical University of South Carolina (1979)
University of Pittsburgh, Pennsylvania (1983)
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HONORS AND AWARDS:

Krieg Cortical Discoverer Medal, Cajal Club (1992)

Jennifer Lund is an anatomist who elucidated the organization of feedforward and feedback circuits and projections in neocortex, first observed the exuberance and pruning of dendritic spines in the primate visual system, and described the patterns of lateral connectivity that are a universal feature of cerebral cortex.

Jennifer S. Lund

I am definitely not from a line of scientists. My parents were artists and my siblings are also working in the arts, both accomplished potters. In my youth, however, I was intrigued by the natural world, finding both plants and animals visually pleasing and behaviorally interesting. I was curious to find out how things worked—that is, mechanical devices or living things. However, I suffered from a complete lack of mathematical understanding. In part this was because my all-girls school could never keep—or even find—adequate math teachers. If, however, the concept or data were presented in a visual form—a graph, histogram, or three-dimensional plot—I usually easily grasped its meaning. This lack of mathematical knowledge, an essential tool of science, made physics and chemistry sheer torture, despite my interest in them. Also, the manner in which they were taught me, as rote learning, was totally alien to the way my mind worked. However, my teachers of zoology and botany were admirable and always presented the biological world as a series of puzzles to be solved and rational solutions that nature had devised for natural biological problems. That, and the beauty of the biological materials, persuaded me in their direction.

My botany teacher was particularly outstanding and I will always remember her discourses on the evolution of reproduction in plants. However, there was strong pressure in my school for students to go to medical school, and zoology was perceived as having more intrinsic 'worth' than botany in this regard. However, being resistant to being useful when it came time to choose a field of study at university, it was zoology, not medicine, that I chose. I received little advice as to which were the best universities in England at which to pursue this interest. Oxford and Cambridge were not available to me since I had failed dismally to master Latin—another subject taught me by rote learning—which was required by both. While applying and being accepted by many other Institutions, fate must have decided to be kind because I accepted a place at University College, London (UCL) in the zoology department. Peter Medawar was head of the department, Maynard Smith, Brian Boycott, Alex Comfort (*Joy of Sex*), and G. P. Wells (son of H. G.), among others, comprised an illustrious faculty. Since only 12 students were accepted per year, and the courses were taught on 3-year rotations so that students from all 3 years were taught together, it was an unparalleled learning experience. There

was still too much rote learning for my liking, but much of interest in terms of biological problem solving. To my amazement, botany, my second subject, was presented at a level of excruciating dullness and no one on the faculty appeared to have heard of the excitement that had been clearly revealed to me in high school. This goes to show that one should not judge the interest of a topic by the teachers one has!

One of my tutors in zoology was Brian Boycott, and I was introduced by him to the visual centers of the mammalian brain. More important, he helped me to reach the next stage in my career. Having achieved a first-class degree, much to my surprise and probably that of my tutors, and filled with disbelief that this fairly represented my academic abilities, I paid a visit to the office that gave career advice to graduating students. I was advised to take a secretarial course. Stunned, since most of my class at school had left at the age of 15 to do just that, I asked whether that was the advice given to the male students. 'No' was the answer; they were advised to take management courses. I returned to a suggestion that Brian Boycott had given me, which was to take a position as a technical assistant to a research faculty, Jack Downer, in the department of anatomy. I applied and was accepted for the position; meanwhile, I set aside a letter offering a scholarship to undertake a Ph.D.; I was totally unsure as to what such further study entailed.

On my first day in Jack Downer's laboratory, I was detailed to wash up a sink-load of dirty glassware. Having begun on this task with the enthusiasm of a new recruit, I was shocked to be told sternly by a head that peered round the door frame that I was using too much washing-up liquid! Tender shoot of a researcher that I was, I puzzled over this remark, wondering what rationale lay behind it—was it that I had so contaminated the glassware with soap and it would now ruin other's experiments, or was the department so hard up for funds that they even monitored the amount of dish-washing detergent? Later, I discovered it was a Ph.D. student who, being intrigued to see the new female on the floor (probably the only female for many floors), had looked around the door and, being embarrassed to be seen by the object of his curiosity, had put on the fiercest act he could think of quickly. He, Ray Lund, later became my husband; we believe this came about because there was no other unmarried female within a considerable distance and we were both far too busy to go in search of anyone else. It worked out well, particularly since Robin Weiss, a fellow student from zoology, gave us a copy of the *Kama Sutra* to encourage and inform us. Ray has been my most important scientific mentor as well as the kindest of husbands—a hard double act to achieve and still remain married!

Jack Downer, trained by Roger Sperry, was working with split-brain monkeys, examining the phenomenon of interhemispheric transfer of visual memory. He taught me the surgical procedures involved, and after

the first year as his technician I became a Ph.D. student since I was intrigued to develop new experimental paradigms rather than carry out the routine histology he had hired me to do. I developed a truly baroque thesis project involving teaching split-brain monkeys to adapt their reaching behavior to compensate for vision deviated by a prism worn over one eye (the other occluded); the aim was to determine if they retained the compensation when vision was switched between the eyes to the side of the brain lacking the training experience and to an arm that was run from the opposite hemisphere: They do. My thesis writing was a difficult task; J. Z. Young was my official supervisor and he was scathing in regard to my ability to write good English, sending me away to rewrite and to read the *Times Literary Supplement* as a model for how to write. He was of course correct about my inability to write clearly, but afterwards I discovered this was also a gambit he used to send away students when he was too busy to read their efforts. My thesis project was one of those projects in which in the thesis defense one says, 'If I had known what I know now I would not have done it that way.' Nonetheless, I duly received my thesis, more I think as an award for effort expended than for solving any important aspect of visuomotor control. It also helped that there was a pile driver running outside the exam room so that the defense was cut short after the examiners and I became exhausted from shouting questions and answers at each other.

Another student who joined the Downer lab during my time there was Semir Zeki, who came with his personality fully developed to cause sparks to fly. In fact, the whole anatomy department was a scintillating place to be; the faculty was highly talented, and for neurobiology the department was probably the best in the world at that time. J. Z. Young was hard at work on the octopus brain and had clearly encouraged the development of a group of scientists and visitors who had much to contribute to the development of neuroscience as a field and visual system and cortical anatomy in particular: Ray Guillery and Ray Lund, who were working on visual pathways and their development; George Gray, Marc Colonnier, Peter Ralston, and Lesnick Westrum, who were developing electron microscopy of synapses and other elements of the nervous system; and Keith Webster, Lodwick Evans, and Brian Cragg, who were investigating basal ganglia, nerve regeneration, and neural development. Some developments were ahead of their time; in the attic was a giant early computer, run apparently by clocks, that its developer (A. Taylor) assured us had the intelligence of a 3-year-old child. However, he became less convinced of this when he became a father. Later, my husband was undiplomatic enough to point out to the American Anatomical Association, as he received the honor of their 'Most promising young anatomist' prize, that nearly all the recipients to that date had been trained in J. Z. Young's department in the United Kingdom. I believe what made it an exceptional training ground

was the very English habit of gathering for morning coffee and afternoon tea at set times. This meant that the latest findings in the department were avidly discussed and new literature was commented on; this was an exceptionally useful way for the students and faculty to share ideas, excitements, and opinions.

As I finished my thesis, it became apparent to my husband, who was by then a faculty member in the Department of Anatomy, UCL, that there was very little opportunity to move to new jobs in the United Kingdom. The few advertisements that there were for academic positions in our field generally terminated with the words 'Only medically qualified gentlemen need apply.' My Ph.D. husband believed that this disqualified him on at least two counts; of course, for me it was clearly the knell of doom. Therefore, at the urging of Jim Sprague, in 1966 and 1967 we spent a year in Philadelphia at the University of Pennsylvania. We were overwhelmed by the kindness of the distinguished neuroscience community—not only Jim Sprague but also Elliot Stellar, Bill Chambers (under whose watchful eye I put finishing touches to my thesis studies), John Liu and Michael Goldberg in anatomy, Alan Laties in ophthalmology, Sol Erulkar in physiology, and many others went out of their way to see that we had the greatest introduction to America and its scientists. Also, among the lively neuroscience students was Murray Sherman, who was even then a notable vision researcher.

Unable to decide whether we should return to the United Kingdom, we took a further year of leave and, at the urging of Peter Ralston, our former colleague at UCL who was now a faculty member of the anatomy department at Stanford University, we drove across America in our second-hand but unbeatable Dodge Dart to Palo Alto. Here, in 1967 and 1968, I learned electron microscopy from Ray and began to examine the cortex of the rat. Because I was interested in the function of the corpus callosum, I was determined to find out what neurons these projections terminated on and what the callosal terminals looked like. The process of carrying out this study was particularly absorbing since everything was new; there was little information regarding the basic synaptic organization of the cerebral cortex at that time. Memories of discussions around the teacups at UCL and the information provided by Ray that neural pathways took to degenerate after lesions, in addition to the knowledge that the terminals of the severed connections could then be recognized by darkening of the dying terminals in osmium fixed material, became of great importance. When I presented this work at the American Anatomical Association meetings, I was overjoyed to be congratulated by Marc Colonnier, who told me of his own observations on cortical synapses (his paper was already in press), and I felt reinforced in my work by the agreement between our observations. At the same time, I was working with monkeys and had discovered a great colleague and another former student of Roger Sperry—Charles

Hamilton. Charles agreed to join a project to determine if interocular transfer of discriminations based on direction of motion of visual stimuli occurred in the split-brain monkey. They did not, suggesting that discrimination of motion is dependent on cortical mechanisms, as had been shown earlier for pattern.

This was a strange time in America. The Vietnam war was looming and the students were increasingly distracted by the factors that it involved. Stanford students abandoned the campus by 5.30 PM, leaving it eerily silent. When we asked what went on in the evenings, they asked us 'what were we into?' On further enquiry there appeared to be a rich choice of illegal or immoral activities that the naive Lunds felt too abashed to explore! Therefore, as the year neared its end, and again at the urging of a former colleague and great friend from our UCL days, Lesnick Westrum, we were off to Seattle to a proper faculty position for Ray and uncertainty for me. Eventually, a soft-money research position was found for me in the ophthalmology department, headed at that time by Karl Kupfer. My appointment was vigorously supported by Anita Hendrickson, who had heard my talk on cortical synapses at the anatomy meetings. Anita proved to be one of the kindest and supportive of colleagues, and during the next 11 years in Seattle my academic life benefited immeasurably from her input.

Carl Kupfer was anxious to apply for program grant funds and we were all roped into contributing research proposals in the area of the primate visual system. I was allotted the visual cortex, and this area has remained my principal research topic for the whole of my career. It is a region of the brain worthy of attention, being of extreme complexity but orderly in its anatomy. Its other benefit is that many others have also been exploring its function as well as its anatomy. It is certainly the best known region of cerebral cortex today, and there was at that time clear interest in its exploration as demonstrated by the work of David Hubel and Torsten Wiesel as well as by younger members of their laboratory, Simon LeVay and Charles Gilbert. At that time, the tools available for studying single neuron morphology were very limited, so I decided for my own interest to use one of the oldest neuroanatomical methods—the Golgi technique. After some dismal first attempts (bad Golgis are the most depressing material), I managed to obtain some glorious impregnations using the Golgi rapid technique in young macaque cortex. What a revelation! Although Cajal's work and that of Donald Sholl had alerted me to the kinds of neurons I might see, there is nothing to compare to actually seeing it through a microscope and realizing that that very same structure is in your own head, looking at it, and puzzling over its own organization. However, wondering over the beauties of nature does not get one very far in exploration of how the cortex might function, so the next years passed quickly indeed as I tried to trace within the primary visual cortex the patterns of

intrinsic axonal relays. The rationale of these studies was to consider these projections as either the serial forward running relays of two kinds of thalamic information, which we knew enter the cortex and terminate in different divisions of layer 4, or feedback projections along the same intrinsic paths.

Missing at that time was any detailed knowledge regarding how information left area V1 to travel to other cortical areas or to subcortical sites. This essential information became available to me through work with Anita Hendrickson and Ann Bunt, a new colleague in ophthalmology. Anita had been exploring new retrogradely transported anatomical tracers and thought that they might be used to label cells of origin in the visual pathways between retina, thalamus, cortex, and superior colliculus. A colleague in the chemistry department extracted the enzyme horseradish peroxidase from raw horseradish roots, and the pungent fumes promptly emptied the building! However, the resultant brew worked well when injected into the brain with the considerable help of Al Fuchs, who had no idea what we were up to but who volunteered to help us locate via physiological recording the superior colliculus and lateral geniculate nucleus (LGN) in the anesthetized monkey so that we could place injections. For my part, given the cortex from these animals, the finding that the efferent cells projecting to different destinations were sequestered to different cortical laminae provided another key element in understanding the organization of cortex and made sense of the intrinsic relays I had been describing—the internal pathways were leading to different sets of efferent neurons.

The presence of a primate center at the University of Washington was a major benefit to the research we were doing at that time and especially important to developmental studies of the primate visual system. I had the opportunity to collect Golgi material from a series of pre- and postnatal animals and began to search for significant stages in the early development of visual cortex. The brains were listed in order of age, but I became worried that there had been an error in the dating as I examined the material. I had expected that spine populations on the dendrites of excitatory neurons, which are sites of excitatory synapses, would gradually increase in number as the animals matured, perhaps with an acceleration in spine formation at birth but then increasing in number to a stable adult density. Instead, I seemed to be seeing a relatively low number around birth, with a sudden escalation in spine number a week or two after birth which over time eventually produced such a high density that the neuron's dendrites could resemble thickly piled carpet—with a spine density so high that it was impossible to count them. Mysteriously, as the animal aged, the spine density decreased again to eventually the same level seen at birth, but now the animal was sexually mature. I found this immensely interesting. At that time there was keen interest in the early postnatal

period of visual maturation. The fact that animals reared with various paradigms of visual deprivation during this so-called critical period showed marked deficits in visual function and anatomical changes in the form of changes in at least ocular dominance domains had been demonstrated by LeVay, Wiesel, and Hubel, which made it especially interesting that this also appeared to be a period of supernumerary synapse formation and loss. It appeared to be a phenomenon resembling that observed by those investigating maturation of the neuromuscular junction, which also undergoes a period of supernumerary synapse formation and loss during maturation. I discovered that Brian Cragg, who had since become a sheep farmer in Australia, had described using electron microscopy a period of superabundance of synapses in kitten postnatal cortex, so it appeared that this was an event common to other species. It has since been shown that it is a universal phenomenon across cerebral cortex, with differences in timing between layers and between areas of cortex.

The years in Seattle in the mid–1970s were very happy ones. My two sons were born there, and Ray and I found the marvelous landscape in that region a constant source of pleasure. We bought a tiny cabin near the shore on Whidbey Island in Puget Sound and we and the children had many splendid weekends and holidays there. Ray had an enthusiasm for rowing, and we acquired a small rowboat; he and the children would row off and become tiny specks in the distance while I mentally rang my hands and imagined widowhood and children's graves. The sea water was as close to freezing as it can get, even in midsummer, but as the tide came in over the hot rocks the top 6 inches warmed up nicely so swimming was possible so long as no portion of anatomy sagged into the cold layer below. We dragged the kids up mountains among the spring flowers, carrying them while small enough and then, when heavier, cajoling and tempting them along with bribes of food and amusements. We dreamt up an Olympic event in which the paired athletes are given two tiny toddlers (no carrying allowed) and the race is won by those who arrive first at the finish line with all members of the team in good spirits!

I have been asked if I have experienced discrimination as a woman in science. I must say that, first, I am fairly oblivious to the real world so it might have happened without me knowing. Only two occasions come to mind now (but not at the time) when such an issue may have occurred. In the process of reviewing our department program of research, one distinguished visiting adviser sat down with me and said, 'Now be honest with me Jenny—it was Ray that did the study on EM of the cortex, wasn't it?' I sat nonplussed, wondering if I had heard the question correctly, probably turning bright pink with embarrassment that he should think so little of my skills! The other occasion was one in which I had been asked to address the women students, together with other female faculty members, on the art of balancing work and family. Reluctantly, I agreed, and I led off with

a brief summary of my experiences; all the other speakers then launched into a competitive, ever more dire life experiences exercise, clearly showing me to have been a mere dilettante! Never again—women proved to be my harshest critics.

It was in the late 1970s that Ray and I achieved our first and only sabbatical year. We went to the laboratory of Geoff Henry in Canberra, Australia, and were overwhelmed by both Australian hospitality and the extraordinarily beautiful landscape and bird life. We lived on the Australian National University campus, and every morning flocks of exotic parrots would surround the house—paradise! While the members of the department of physiology were often at war with one another, they treated us with the greatest kindness. Lunch with Peter Bishop was quite an intellectual challenge and discussion of the horopter (the locus in space within which an object must lie for it to appear binocularly fused) over sandwiches was not to be forgotten. The Lunds, however, throve, and while Ray wrote a book I tried to learn physiological recording techniques. This involved about eight monstrous racks of equipment hooked together by a forest of wires. Since we were trying to test projections between areas by the collision technique, it also involved resetting the wiring between the racks each time we applied the test. This was so complex that the head technician had to be summoned to wander around and readjust the wiring each time we were ready. No one understood what he did to achieve this, other than to make himself totally indispensable. This has always been my excuse for why the workings of electrophysiological equipment, like videocassette recorders and computers, remain a mystery to me. Nonetheless, interesting data resulted from the Canberra experiments that showed that the efferent neurons projecting to specific destinations had unique physiological characteristics.

Having a husband who is outstanding in his research field can be a great advantage if one is prepared to have absolutely no pride. Ray has been recruited to many places and each time he has had to admit to having an academic wife who needs to be accommodated somehow. I have been most kindly treated in this regard, and somehow things have always worked out well—even if not initially too promising. We moved from Seattle to the Medical School of South Carolina (MUSC) in Charleston in 1979, where I was made Professor and Director of the Ophthalmology Research Division. It occupied the top floor of a new building, the Storm Eye Institute, and Rosalie Crouch was its sole occupant at that time. She made us most welcome and initiated us into the inner workings of ophthalmology. This took some doing since the department was run at that time by a southerner of Machiavellian temperament and bizarre habits. Despite some stormy times, our research flourished. I was fortunate to have some of the most talented neuroscientists with me—Gary Blasdel, David Fitzpatrick, and Kathy Rockland—and it was a very productive time. Kathy told me

one day that she had what appeared to be an artifact in her tree shrew cortex histology—a curious barring of the staining pattern around an HRP injection site. We realized we were looking at a spectacular, geometrically organized, intrinsic set of connections, which mimicked the pattern of activity visualized in the same species' cortex using 2DG label by Alan Humphrey; this was shown by his physiological work to reflect regions of isoorientation preference in the neuron populations. To find an anatomical connectivity match to that pattern was a real thrill and raised hopes of finding the visual cortex holy grail—the substrates for generation of orientation specificity. While we went on to find different and equally spectacular patterns of lateral connectivity in primate visual cortex, that particular holy grail still evades investigators today. David Hubel and Torsten Wiesel won their Nobel prize at this time, and David was kind enough to come to Charleston on a site visit the day following the news of the prize. He was euphoric and we were later the fortunate recipients of a center grant, aided, I am sure, not only by our evident progress but also by his excellent mood.

Although we were in Charleston for only 4 years, we made considerable progress and everyone seemed to enjoy this most beautiful of American small towns and its exquisite setting in the Carolina marshes. Gary Blasdel and David Fitzpatrick made a good pairing, and their work on properties of neurons in layer 4C and intrinsic patterns of connections was of considerable interest. Gary, technically expert as ever, made a particularly fine contribution in terms of penetrating and labeling via micropipette individual thalamic axons entering the visual cortex—the first time these axons had been individually visualized and mapped—which was an essential piece of knowledge if we were ever to work out how cortical response properties were initiated. Also with me at this time was my graduate student Sharon Mates, who had to split her time between the University of Washington, Seattle, and Charleston, South Carolina—a not inconsiderable feat. She seemed to survive by running marathons and living on a diet of carrots, which no doubt greatly helped her with her EM studies of cortical synapse maturation carried out largely in the darkness of the EM room. Her thesis finished in grand style, and although she subsequently lost heart with neuroscience, she is my most successful student. She has been named as one of the 10 top women in U.S. business and runs a most successful worldwide, vaccine-making company.

In 1983, my husband took the post of Chairman of the Department of Anatomy and Neuroscience at the University of Pittsburgh. I became Professor of Psychiatry (for salary), Professor of Neurology (for space), Professor of Ophthalmology (for old times sake and research relevance), and Professor of Anatomy (to be a member of the graduate school). Despite this schizophrenic state, it worked out very well for my lab and I built

some interesting collaborative ventures with faculty in these diverse departments. I was indeed fortunate again to have some outstanding colleagues. Gary Blasdel came with me to Pittsburgh and discovered the art of optical imaging of cortical activity patterns in the anesthetized animal using a very sensitive television camera. His companion in this work was Guy Salama, an expert in heart muscle and knowledgeable in regard to the use of voltage-sensitive dyes. Gary came to me with maps of the orientation domains, but we agreed no one would believe them, even with confirmation of their reality using unit recording. I felt uncertain of their reality, so I suggested he try instead for ocular dominance domains, which were readily confirmable by anatomical techniques. No sooner said than done—back he came with unmistakable ocular dominance maps, and the field took off. Amiram Grinvald, who had spent many years exploring cortical activity and voltage-sensitive dyes using diodes, was understandably upset when Gary presented his work at the Society for Neuroscience—the large field-imaged maps were indeed spectacular—but time has healed those wounds and Amiram's lab went on to demonstrate that even the intrinsic changes in reflectance of the cortex when active would produce good images without voltage-sensitive dyes. Today, many labs are producing excellent imaging studies, and David Fitzpatrick, my former colleague, is now one of the frontrunners in this field as well. The optical imaging maps allowed us to test the functional allegiance of the lateral connectivity fields in the superficial layers of cortex, and another excellent colleague, Takashi Yoshioka, worked with Gary Blasdel to examine this aspect of cortical organization. It became clear that the lateral connections, when labeled by anatomical tracer placed at a single, small cortical point, tended to establish reciprocal links between the injection site and a field of surrounding points of like functional kind.

At this time I had begun in earnest a Golgi study of the interneurons (generally inhibitory) within the primary visual cortex of the macaque. This proved intriguing; not only were there many different kinds of neurons but their axons appeared to participate in interesting ways in interlaminar circuits that related to those I had previously outlined for the excitatory pyramidal and spiny stellate neurons. Moreover, it was becoming apparent to us that patterns of lateral connectivity were scaled to match the physical size of individual pyramidal neurons and elements of the inhibitory neuron organization. This suggested that there might be a clear set of rules that underlay the geometry of both anatomical cortical connectivity and fine-grain functional parcelation. Curious as to whether this type of organization of patterned lateral connections was peculiar to just the visual cortex, we tested other regions of cortex with the same approach of small tracer injections and found indeed that it was a universal feature of cerebral cortex.

One day, I received a call from another faculty member in psychiatry, David Lewis, who asked me to look at a slide he had made of prefrontal cortex using immunocytochemical staining for corticotrophin-releasing factor (CRF). He explained that layer 4 was full of small carrot-shaped objects and asked me to take a look at it and make a guess as to what they might be. To my surprise and delight, they appeared to be the axon cartridges of a peculiar sort of interneuron known as a chandelier neuron, which I knew well from my Golgi studies and from Cajal's descriptions. This GABAergic neuron is of particular importance in cerebral cortex since (as shown by Peter Somogyi) it controls the output of the pyramidal neurons via synapses covering their axon initial segments. However, my question to David was how could it be that this neuron appeared to be restricted to layer 4 of prefrontal cortex when one would expect pyramidal neurons at all depths. Our later Golgi studies showed that the chandelier neurons occurred at all depths, and so did the pyramids, but the work raised questions as to whether immunocytochemistry could be used to demonstrate the presence or absence of particular neuron classes. David proved to be an ideal colleague, and some of the ideas that had worked well on the visual cortex we tested on the prefrontal region, with good results. Particularly interesting to me was that the system of lateral connections in prefrontal cortex established fields composed of repeating stripes of terminals around the injection site, which implied that the constraints leading to these patterned connections could differ between cortical regions.

Pittsburgh was an interesting city in which to live. Andrew Carnegie had built his industrial empire there and it had been the heartland of American steelmaking. When we arrived the steel mills had almost all ceased operation. The city and particularly the nearby small towns were faced with a massive collapse in jobs with much hardship involved. During the time we were there, it was gradually recovering and the city was a green and pleasant place with much going on. We particularly enjoyed the magnificent art gallery, and the children were suitably impressed by Carnegie's dinosaur collection next door in the museum. Much music making was occurring in the city and, since my husband is a fine pianist, much occurred at home too. We bought a small cottage in the Allegheny Mountains, gloriously wooded during summers with the splendid thrills of whitewater rafting at Ohiopyle State Park, where rivers converge to a rocky gorge, and threatening during the snowy winters when the kids learned to ski. I was an expert in après ski, having scared myself considerably by setting out to cross-country ski for the first time with my sons and ending up head down in a snow-covered thicket of rhododendrons, considerably off the track. I viewed it as a warning that God had not intended me to ski.

A special pleasure to Ray and me was the rapid development of the neuroscience community at the University of Pittsburgh, encouraged by

the formation of the Center for Neuroscience that we helped found and headed in succession. This organization was truly a community enterprise, run with very little funds but much enthusiasm. The intake of graduate students accelerated, and new faculty were added throughout the campus. Eventually, it spread to establish links with Carnegie Mellon University, and it continues today as strong as ever, which pleases us greatly. However, despite being happily occupied in Pittsburgh, my husband was being urged to consider a move to Cambridge, England. He was invited to both head the new MRC Institute for Neural Repair that was to be built there and to be professor of anatomy. This proved tempting to him and we visited Cambridge. I was offered a position in physiology, which despite some unease over primate usage seemed to offer me a setting suitable for continuing research. Ray left for England ahead of me since our younger son, Simon, had still to finish high school the next summer. Meanwhile, I submitted a grant to MRC through the Cambridge University Grants Office to support my research there and planned the layout of my new lab with the Cambridge University architect. About 3 months before I was due to move to England, I visited Ray to find him very upset. It transpired that he had been told that my faculty position had 'disappeared'! I immediately traveled to London and expressed interest in a faculty position that had been offered to me earlier by Adam Sillito at the Institute of Ophthalmology, then at Judd Street in London. All seemed well at the institute, which had excellent colleagues and a new building virtually completed, so I accepted the position and returned to the United States. To this day, no one at Cambridge has ever contacted me either to enquire why I did not arrive or to explain what happened. The only person there who expressed regret was the grants office head who, on learning that I wished to transfer my MRC and National Institutes of Health grants (which were newly funded) to London, said what a pity it was that Cambridge would lose the money. Sometimes academia is a very strange place indeed.

Life in the United Kingdom brought new colleagues and collaborations and yet continuity was maintained. Jonathan Levitt, who came with me from Pittsburgh, flourished and completed some beautiful studies on V2, of both its extraordinary intrinsic connectivity and its patterns of pulvinar connections. His physiological studies were also most fruitful, with analyses of surround modulation of the classical receptive field in V1 neurons (which now enables us to compare the scale of the intrinsic connectional field with the scale of both the classical receptive field and the surround modulatory field) and of color and motion in area V3 (with Carl Gegenfurtner and Daniel Kiper). Alessandra Angelucci has brought elegance to the lab in terms of the art of tracing cortical connections and is laying the foundations for a real understanding of the structure and logic of interareal feedforward and feedback links between the early cortical areas. Chris Tyler and Achim Rumberger have patiently explored the

marsupial and rat cortices with me, showing that there is a universality between the cortex of all mammals in the neuron types and connectivity patterns they contain—the monkey is not a special case.

We also maintained our relationship with Gary Blasdel, currently at Harvard, by means of a Human Frontiers grant and came to know better Klaus Obermayer at the Technische Universitaet, Berlin. Klaus had worked with Gary on an elegant series of theoretical and statistical analyses of the optical maps of monkey visual cortex, and he was interested in working with us to develop neural models that explored how the anatomical connection patterns in primary visual cortex could underlie the functional patterns mapped or recorded in the region. I believed that such models should begin with the entry of thalamic axons into layer 4 and that we should try to explain the generation of the simplest properties of receptive field size and contrast sensitivity within layer 4. Once this foundation had been firmly laid, it should be possible to use it as a base to attack more difficult issues. This collaboration has yielded some interesting predictions. For instance, the existence of two populations of thalamic M axons entering layer 4 but with different depth distributions (seen by us during Gary Blasdel's axon-filling experiments) may underlie the marked changes in field size and contrast sensitivity in neurons lying at different depths through the upper part of the thalamic input layer. Also, it became clear from modeling that the presence of lateral reciprocal connections makes unique demands on the accompanying inhibition. It appears quite likely from these models that in the monkey anisotropic lateral connections, observed in layer 4C, can begin to generate orientation specificity for the neurons in the layer rather than its arising from convergence of LGN fibers as may be the case in the cat. These modeling studies, carried out by Ute Bauer and Peter Adorjan, have been a particularly exciting new venture in our work.

When I was asked to write this chapter, I believed that I was too young and certainly lacking the distinction that other authors bring to this series. It also occurred to me that there might have been a need for more women to be represented, and we are a bit scarce in my age group. However, I am flattered by the invitation and believe that the work of all my younger colleagues should be celebrated here for its excellence and as the spur for my own efforts. They will, I am sure, be asked to write their own contributions in due course. I also remark on the impact that the Society for Neuroscience has made on my academic life. That impact has not been so much through serving as an officer for various functions of the society but rather in the extraordinary influence of its annual meetings. The sheer scientific energy and extent of interchange of ideas and discussion at these meetings is of immeasurable importance to the field and a phenomenon so extraordinary that it should be better appreciated by the rest of the world. I feel fortunate to have been present at these meetings

throughout my career and to have witnessed the growth and current power of this discipline firsthand through these meetings. I now work for the International Brain Research Organisation and appreciate more fully how the energy of the discipline is spread internationally. I hope we will be able to continue this momentum in neuroscience for many years to come.

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