# Ranier (Ray) W. Guillery

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by

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Ranier (Ray) Guillery was a major figure in the field of Neuroscience. He was remarkable along many dimensions: his research output represents a highly productive and influential body of work; his work profoundly advanced our understanding of the related fields of development and thalamocortical functioning; his work was highly imaginative and insightful; and he was a cherished colleague and role model for his many former students and friends in the field.

## Early Life

Ray was born on 28 August, 1929, in Greifswald, Germany, where his father had a university appointment as a pathologist. Ray then moved with his mother to Berlin when he was three years old, soon after his parents divorced. Ray's mother was born Jewish (his father was not), and although she became a Quaker, the Nazis considered her to be a Jew. Luckily for us, this fact suggests a certain level of drama leading to Ray's survival and his eventual significant contributions to science. These events possibly stamped in Ray a cynicism of authority, in academic life and beyond, but suffused with his humor, never hampered his scientific and professional progression and accomplishments. He left Germany with his mother in the fall of 1938, and after an odyssey that saw him spend time in the Netherlands and Switzerland in boarding schools apart from his mother, who had landed in London, he eventually made it to England.

Ray spent his early English years mostly in boarding schools and actually had rather little time with his mother, who lived in London. He occupied much of his vacation and other times away from school as a houseguest in the home of Wilfrid E. LeGros Clark, a famous neuroanatomist who by then was the Oxford Professor of Anatomy. Ray's time with LeGros Clark undoubtedly influenced his ultimate career choice.

## Higher education

Ray won a scholarship to study medicine at University College London (UCL) from which he received a B.Sc. in 1951. Among his teachers there were J.Z. Young and Bernard Katz. At some point during his medical training, he realized that he did not want a career as a clinician and rather gravitated to biomedical research. Towards that end, he entered a PhD program at UCL under the tutelage of J.Z. Young. His main interest centered on the hypothalamus, and his thesis involved a quantitative count of axons in the fornix, a fiber pathway between the hippocampus and mamillary bodies of the hypothalamus. He received his Ph.D. in 1954.

Faculty positions

After his PhD, Ray stayed on at UCL as a faculty member until 1964, at which time he moved to the USA where he accepted a faculty position in the Department of Anatomy at the University of Wisconsin. There he founded a neuroscience graduate program and fostered faculty with interest broadly in neuroscience and visual neuroscience. In 1977, he moved to become Professor in the Department of Pharmacology and Physiology at the University of Chicago. There, he became the founding Chair of the Committee on Neurobiology, thereby starting the first PhD granting graduate program there devoted to Neuroscience. In 1984, he returned to England to become Thomas Lee's Professor and Head of the Department of Human Anatomy at the University of Oxford. In 1996, at age 65, he moved back to his old Department of Anatomy at the University of Wisconsin with the title of Visiting Professor and Senior Scientist. Then, to be closer to his daughter, who had settled with her husband in Istanbul, Turkey, he moved there in 2006 to become Visiting Professor in the Anatomy Department of Marmara University. Finally, in 2010, he returned to England as an Honorary Emeritus Research Fellow of the MRC Anatomical NeuroPharmacology unit at the University of Oxford. He remained in that position and enjoyed a productive writing period until days before his passing.

Family life

In 1954, Ray married Margot Pepper, who at the time was completing her medical degree. Four children were born to Ray and Margot during his time at UCL. Peter John Guillery, born on 6 January 1957, is an architectural historian living in London. Nigel Robert (known as Edward) Guillery, born on 18 June 1958, is a pediatric nephrologist living in Portland. Richard Philip (known as Phil) Guillery, born on 25 March 1960, works for sustainable forestry as a Director at the Forest Stewardship Council and lives in Minnesota; and Jane Louise Guillery, born on 20 September 1963 and now Jane Kandur, is a teacher and language translator living in Istanbul.

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Scientific contributions

Ray was an extraordinarily productive and insightful scientist. At the beginning of his career, Neuroscience was in its infancy as a recognized profession, and the field as such was distributed amongst the more established and recognized divisions at the time, such as Anatomy, Physiology, Psychology, Pharmacology, etc. The subdisciplines within Neuroscience (e.g., Neuroanatomy and Neurophysiology) generally ignored one another. However, whereas Ray's early work could be characterized as Neuroanatomy, he always had a holistic theoretical framework that informed his approach, so that rather than positioning himself as a descriptive anatomist, Ray always interpreted his findings more broadly and queried their meaning in physiology and behavior.

Ray trained at UC-London with J.Z. Young, and in collaboration with George Gray and Brian Boycott, was the first to describe symmetrical and asymmetrical synapses using the new technology of electron microscopy. Broadly interested in the cytology and connectivity of neurons, Ray's early work concentrated on hypothalamus and its connections, variously the cytology of the leech nerve cord and of connections in sensory systems of other lower vertebrates (Boycott et al 61;Gray and Guillery 61;Boycott and Guillery 62;Gray and Guillery 63a;Gray and Guillery 63b). Ray was drawn to and focused on thalamus and thalamocortical relationships, including development thereof, and used the mammalian visual system as his chief model for investigation. His major contributions can be placed into four main categories: investigation of visual pathways from retina to cortex, investigation of the development of these pathways, studies of the defect in these pathways associated with albinism, and theoretical considerations of thalamocortical relationships.

*Studies of retino-geniculo-cortical pathways*. Most of Ray's contributions on this topic were based on the cat model, although other species were also studied. He was an early practitioner of electron microscopy, and he used this to good effect to unpack circuitry of the lateral geniculate nucleus (Guillery 69a;Guillery 69b). His work classified and defined the source of the various synaptic profiles in this thalamic nucleus, and he established the surprising finding that the functionally dominant input from the retina produced surprisingly few synapses onto relay cells. He then extended many of these observations to the monkey (Colonnier and Guillery 64;Guillery and Colonnier 70). Likewise, in a landmark Golgi study, he defined the classes of relay cell and interneuron in the lateral geniculate nucleus of the cat (Guillery 66). Ray also redefined the laminar patterning of the cat's lateral geniculate nucleus (Guillery 70;Hickey and Guillery 74) and pointed to complexities in lamination of the human lateral geniculate nucleus (Hickey and Guillery 79).

*Studies of retino-geniculo-cortical development*. Ray's developmental studies concentrated on development of the visual pathways in kittens, particularly with respect to the effects of early visual deprivation. Arguably, his most important contribution here was his rigorous demonstration of the role of binocular competition in development of the visual pathways, that is, competition between pathways related to each eye in the formation of enduring connections in thalamus and cortex. He first showed that cell shrinkage in the deprived layers of the lateral geniculate nucleus in monocularly deprived cats was limited to the binocular segment (Guillery and Stelzner 70). This showed that the deleterious effects of deprivation only occurred in regions where the deprived eye would have to compete with the open eye for synaptic connections; in deprived monocular regions, where the deprived eye was by definition at no competitive disadvantage, development proceeded relatively normally.

In an ingenious extension of this, he created an artificial, central monocular segment for the deprived eye by placing a central retinal lesion in the open eye. Again, deprived geniculate cells grew to normal size in the natural and artificial monocular zones of the lateral geniculate nucleus (Guillery 72). Finally, in collaboration with one of the authors (SMS), he extended the finding of normal development related to the natural and artificial monocular zones using electrophysiological and behavioral approaches (Sherman et al 74;Sherman et al 75;Sherman and Guillery 76).

Staring in the late 1970s, Ray oversaw a swathe of studies on the development of the visual pathways, spanning studies on abnormal sprouting of retinal afferents (Robson et al 78), development of layers in the lateral geniculate nucleus (Guillery et al 85), and the development of retinogeniculate afferents in the kitten. He also analyzed retinal representations of axon order in the optic tract (Torrealba et al 81;Torrealba et al 82), and even though in the adult, this and the other developmental studies laid a foundation for cellular and molecular studies by his trainees and the field.

*Studies of visual pathways in albinos*. Albinos have long been known to suffer visual difficulties, but these were usually explained by optical deficiencies: lack of pigment means that the retinal image is much degraded by light scatter. Ray showed that there was an additional, heretofore unappreciated explanation: retinofugal projections in albinos are aberrant. In the 1970s, Ray demonstrated that albinos of all mammalian species, from Siamese cats to humans to white tigers, show abnormal patterns of nerve crossing at the optic chiasm, with resulting abnormalities in vision, and then discovered how the brain manages this abnormal visual input. He and Jon Kaas first demonstrated abnormalities in connectivity in the Siamese cat (Guillery and Kaas 71), which has a thermolabile form of albinism. They demonstrated that a region of geniculate lamina A1, which normally receives retinal input only from the ipsilateral temporal retina, instead is also innervated by the contralateral temporal retina. Ray and colleagues extended this basic observation to a number of other species: tigers (Guillery and Kaas 73), mice (Guillery et al 73), minks (Sanderson et al 74), axolotls (Guillery and Updyke 76), ferrets (Cucchiaro and Guillery 84), monkeys (Guillery et al 84), and even humans (Guillery et al 75). In an important extension, Ray and Jon Kaas also showed that the defect in albinos affects cortical circuitry as well and thus likely disturbs vision (Kaas and Guillery 73). The decussation defect at the optic chiasm of albinos was essentially the first developmental genetic aberration identified in higher mammals and is a paradigm for how genetics regulate systems neuroscience.

*Theoretical considerations of thalamocortical relationships*. Starting in 1996, Ray and one of the authors (SMS) wrote a series of theoretical suggestions for new ways of looking at thalamocortical relationships. This led to 10 review articles and book chapters (Sherman and Guillery 96;Sherman and Guillery 98;Sherman and Guillery 02;Guillery and Sherman 02a;Guillery and Sherman 02b;Sherman and Guillery 04a;Sherman and Guillery 04b;Guillery and Sherman 11;Sherman and Guillery 11;Sherman and Guillery 14) and three monographs (Sherman and Guillery 01;Sherman and Guillery 06;Sherman and Guillery 13).

Together, they developed three novel ideas. First, they classified glutamatergic pathways in thalamus and cortex as drivers or modulators, suggesting that only the subset of drivers (e.g., retinal input to geniculate relay cells) carries basic information, whereas modulatory input (e.g., layer 6 corticogeniculate input) serves to modulate the processing of driver input. Second, they identified a novel form of corticocortical communication: layer 5 of a cortical area projects to a thalamic nucleus that relays this input to another cortical area, and these transthalamic circuits connect cortical areas in parallel with direct corticocortical connections. Third, because driver inputs to thalamus often if not always arrive via branching axons with the extrathalamic targets often being motor structures in the brainstem, they suggested that these inputs serve as efference copies for motor command generated by cortex.

The final gift of Ray's broad and important oeuvre is a new book entitled "The Brain as a Tool," the final page proofs of which were received days before he died. This book will be published in fall, 2017, by Oxford University Press. In this monograph, Ray makes an ambitious, and, we believe, successful, attempt to correlate details of thalamocortical circuitry with higher cognitive functions. Ray says it best, so to quote from his preface to the book:

> "….this book, and the title is an attempt to see how we depend on using the brain, its nerve cells and neural pathways, to learn about our interactions with the world. The brain on its own can do nothing. We use our brains to interact with the world. It is not until we start moving about, moving our eyes, or our fingers, that we can start using our brains to learn about the world by interacting with it. If we want to understand animals including ourselves and each other in health and disease, we need to understand the neural pathways and their functions…. That is the focus of this book: to raise answerable questions about living brains and identifiable intercommunicating nerve cells."

## Service and Honors

Ray served in a number of important service positions. In addition to serving on various editorial boards and grant reviewing committees, Ray was the Editor-in chief and founding editor of this journal and a member of editorial Boards of *Journal of Neuroscience* (section editor), *Journal of Neurophysiology*, *Journal of Neurocytology*, *Journal of Comparative Neurology*, *Neuroscience*, *Journal of Anatomy*, *Visual Neuroscience*, and *Neuroembryology and Aging*. Ray served as Treasurer of the Society for Neuroscience, and President of the Anatomical Association of Great Britain and Ireland. Ray was named a Fellow of the Royal Society in 1983.

## Concluding Remarks

Ray’s gifts to us include his critical eye and intellectual rigor, done with the highest note of scholarship, and often suffused with humor even as he was tough. He let us develop independently, insisting on not including his name as author on studies fully done in his lab and cultivated by him. He also posed issues and questions, like a latter day Ramon y Cajal, before he or the field had any knowledge of molecular mechanisms (e.g., (Guillery et al 95).

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Ray’s modesty, interest, sharp intellect, humor and selflessness made him unique as a person, a scientist, and a mentor. He loved opera, gardening, woodworking, cooking, and traveling. He also enjoyed a good dinner with friends during which history, art, philosophy and science were explored and discussed with elegance and humor. During his time in Istanbul, he held long dinners with students and scientists. These meetings helped shape the career paths of many, expanding and adding depth to all subsequent steps taken by them. What made Ray singular was also the way in which he cared for and enabled his mentees to achieve their life goals. He would very kindly allow them to develop their own scientific approaches while gently offering guidance during the process.. He had a stunning way of integrating science and life together as a continuum.

As a scientist, he had a remarkable ability to examine deeply the most fundamental aspects of any scientific puzzle, and he worked on explaining one of the most complex puzzles of all time: How does the brain interact with the world around us and generate conscious experiences? We now look forward to reading about this topic in his upcoming book.

He will be greatly missed.

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