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CLIFFORD LADD PROSSER
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A Biographical Memoir by
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Biographical Memoir

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C. Ladd Prosser

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BY GEORGE N. SOMERO

CLIFFORD LADD PROSSER, AFFECTIONATELY KNOWN as “Ladd” by all who had the great fortune to interact with him during his seven-decade-long career, was a principal catalyst in the development of the broad field of comparative physiology. Born in Avon, New York, in 1907, Ladd either witnessed the early development or, indeed, fostered the very conception of many of the core research areas still being actively studied by biologists who describe themselves as comparative, integrative, or evolutionary physiologists. Workers in this broad area of biological investigation thus owe a major debt to Ladd Prosser, whose curiosity about nature led him to ask penetrating questions that continue to challenge and motivate us. Moreover, and very importantly, he helped to refine a philosophical context—the comparative method—that has enabled biologists to exploit the diversity of nature to elucidate the common, basic principles that characterize living systems.

This short biographical memoir of Ladd Prosser has two primary purposes. One is to provide a description of the scope and breadth of Ladd’s scientific accomplishments, which were foundational for so many areas of physiological study. The second is to describe the character of this remarkably insightful and humane individual in hopes of explaining his

success in motivating and energizing a large cadre of young scientists, many of whom have gone on to become leaders in their fields. We have much to learn from Ladd's formal contributions to physiology—his several books and over 200 research papers—and from the way he stimulated and nurtured others. His approaches to science and to scientists should continue to serve as a role model for others seeking to maintain the vitality of the comparative approach to biology that was the core of his scientific philosophy.

In developing these two themes I begin by acknowledging the assistance I've enjoyed from talking with former Ph.D. students and postdoctoral associates of Ladd and from reading the biographies they have published about their mentor (Hazel and Sidell, 2002; Mantel, 2002). Although I am not an alumnus of Ladd Prosser's laboratory, I had the privilege of working with him for several weeks on board the research ship *Alpha Helix* during the Bering Sea expedition in 1968. Following this we interacted frequently through visits to each other's laboratories, at meetings, and through correspondence. The qualities that accounted for Ladd's remarkable level of success in doing science and in stimulating others became apparent very rapidly. Perhaps the most striking aspect of Ladd's character was a true childlike curiosity about nature, which typically was appreciated at one's very first interactions with him. Ladd claimed that Sunday walks in the woods with his father triggered in him a love of nature and a desire to find out how it works—at all levels of biological organization. Several decades later this curiosity was still there, undiminished and, in fact, probably greatly amplified as he learned about more things to spike his curiosity. As his students have continually remarked, this enthusiasm was contagious for all of those lucky enough to be in the lab with him. On the *Alpha Helix* cruise I had the added privilege of sleeping in the top bunk above Ladd. I can testify that his

enthusiasm continued long into the night, perhaps too long on some nights when my mental stamina (or my stomach's tolerance of a rocking ship) was not up to the standards of this scholar some three decades my senior.

The other remarkable aspect of Ladd's character that quickly became evident was his voracious love of knowledge. He not only was incessantly curious about nature but he also wanted to know what you knew or thought about a myriad of different topics. This desire to learn from others was coupled with capacities for filing away all that he had learned and being able to integrate and synthesize this information both horizontally among disciplines and vertically along the reductionist-holistic axis. Having grown up with many of the fields of physiology and, in some cases, serving as the originator of these fields, Ladd was successful in keeping up on the literature in a way that would be impossible in this day of fragmentation of knowledge and overwhelming output of papers. One of his Ph.D. students, Linda Mantel, commented in her tribute to Ladd, "Scientists with Ladd's vision and breadth of interests aren't made any more, and we are all poorer for that."

FORMATIVE INFLUENCES: FROM WALKS IN THE WOODS TO
POSTDOCTORAL STUDY

Ladd's *Scientific Autobiography and Personal Memoir* (Prosser et al., 2001)," completed shortly before his death, provides many insights into the formative factors that led to his illustrious career. Ladd grew up in a small town in rural New York, where his father ran a general store. The family had hoped that Ladd would follow in his father's footsteps and become a merchant. However, the footsteps that truly mattered were those made along the forest trails, where Ladd's acquaintance with and curiosity about nature set in motion his desire to study biology. These experiences, along with

encouragement from his seventh-grade science teacher, motivated Ladd to enter the University of Rochester, in 1925, as a biology major. A formative event during his undergraduate career was a course he took in physiological psychology, which convinced him that unraveling the underlying neurobiology of behavior could be done more effectively through studying “lower” animals such as invertebrates rather than mammals. This insight no doubt played an important role in the development of Ladd’s philosophy about the comparative method. He graduated from Rochester University (Phi Beta Kappa) in 1929 and went directly to Johns Hopkins University to begin his doctoral studies.

At Johns Hopkins Ladd studied with a leading cellular physiologist, Professor S. O. Mast. Ladd’s wide-ranging interests were manifested even at the onset of his research career. With Mast he studied amoeboid motion and published his first papers on this topic. He did parallel work on the behavior and nervous system of the earthworm, a reflection of his desire to exploit the comparative approach to behavior and neurobiology in his work.

After receiving his Ph.D. in 1932, Ladd moved to Harvard University for postdoctoral study under a Parker Fellowship that stipulated that he must remain celibate for the duration of the fellowship period. At Harvard Ladd studied principally with Hallowel Davis but also interacted closely with other giants in the field of physiology, notably Walter Cannon and Alexander Forbes. The Harvard period saw Ladd further develop his investigations of neurobehavioral phenomena, this time using crayfish as his model system. He discovered the existence of spontaneous, rhythmic neural activity in the central ganglia of this crustacean. In his autobiography Ladd states that this was “one of the most important discoveries I ever made” because of “the prevailing view that all behavior was initiated from outside the organism.” Ladd was

never hesitant to challenge the conventional wisdom when his data indicated that a change in perspective was needed. His studies of the crayfish nervous system yielded yet another surprise: the existence of a caudal photoreceptor that had not been anticipated.

An important component of Ladd's experiences during his periods at Harvard and Johns Hopkins was the summers spent at the Marine Biological Laboratory at Woods Hole, Massachusetts. There he furthered his interests in comparative biology, developed a love of summer retreats to this intellectual epicenter, and in 1934 met his future wife, Hazel Blanchard, who worked in the MBL library. Hazel, of course, could not become his spouse until the constraints of Ladd's Parker Fellowship no longer applied.

Ladd's fellowship support did allow him the opportunity to spend part of his postdoctoral period abroad. In 1933 he sailed to England for study at Cambridge and Oxford universities. At Cambridge he worked with Edgar Adrian, who had received a Nobel Prize in 1932. In Adrian's laboratory Ladd continued his work on earthworm neurobiology. In typical Prosserian fashion, he began to extend his comparative interests even more broadly. To this end he developed a collaboration with John Eccles (a future Nobel) at Oxford University. As those who knew Ladd can attest, his physical energy matched his intellectual energy. Thus, his willingness to commute between Cambridge and Oxford by bicycle was right in character. At Oxford in Eccles's laboratory, Ladd recorded from the sympathetic ganglia of the cat, thus further broadening his expertise in neurobiology.

ACADEMIC POSITIONS AND CAREER HIGHPOINTS

Ladd returned to the United States in 1934. His restrictive fellowship was over. Hazel met the boat, and she and Ladd were married the following day. That same year Ladd

accepted his first faculty position, at Clark University, where he remained through 1939. He received support from the Rockefeller Foundation to develop a research program, which extended his focus on spontaneous nervous activity. Summers were still spent in Woods Hole, where Ladd worked with John Z. Young on the new study system involving the squid giant axon.

Although Ladd prospered during his time at Clark University, he sought a position at a larger university where he could more fully realize his potential in research. Such an offer materialized in 1939: a position at the University of Illinois in Champagne-Urbana, where Ladd was to spend the remainder of his long scientific career. This offer involved a significant piece of negotiation. Ladd's contract specified that he was to teach what would today be called a "service course" for agricultural students. Ladd insisted that he also be allowed to teach a new course of his own design in comparative physiology. This course was to serve as a focus for his development of a synthetic view of comparative physiology that resulted in the publication of his *Comparative Animal Physiology*, which evolved through four editions (1950, 1961, 1973, 1991).

Ladd's career at Illinois was interrupted by the Second World War. Perhaps with some sense of foreboding, he arrived by car at Champagne-Urbana on the day that Hitler invaded Poland. In 1942 Ladd was recruited for the Manhattan Project, and moved his family (now with a young daughter) to Site B of the project, an old brewery in Chicago that the federal government had obtained for research on the effects of radiation on organisms. Ladd organized a group of 150 scientists to work on this poorly understood, yet vitally important issue. His group showed that particular dangers arose from bone-seeking materials like strontium-89. Ladd was one of 69 signatories to the famous Szilard-Einstein letter

to President Truman, dated July 17, 1945, which cautioned on the use of the atomic bomb as a weapon. After the war, Ladd worked briefly on Bikini atoll, where further studies of the effects of radiation were conducted. He also was instrumental in preparing 12 reports on the effects of radiation. This pathbreaking work was an important foundation for the radiation safety standards later developed by the federal government.

Ladd returned to the University of Illinois and picked up the pace of his research program. He also put major efforts into fostering an improved research environment at the university. From the start of his career at Illinois Ladd had worked hard to develop a world-class physiology program at the school. He sought to ensure that physiology was broadly focused and included the study of diverse species, not just mammals. His efforts led to the establishment of the Department of Physiology in 1949 and later to a combined Department of Physiology and Biophysics, which he chaired from 1960 through 1969. He also was a prime mover in developing the neurosciences program at Illinois, for example, through helping initiate the Neural and Behavioral Biology Program.

Despite the altered focus of his scientific work during the Second World War, Ladd's interests in comparative physiology remained strong. He began to envision a textbook in comparative physiology that would serve a number of purposes. It would not only be a comprehensive review of what was known in the field but also would document the importance of examining biological function from a wide evolutionary and environmental perspective. The initial volume of this classic text (1950), which Ladd prepared with the help of four coauthors, succeeded brilliantly and quickly became the standard book in its field. The book was a reflection of Ladd's intellectual strengths, especially his

skills in organization and synthesis. Ladd loved to tell the story about how the organization of the literature for the book involved sorting relevant papers among bushel baskets he kept in the basement of his house. Each basket contained the nucleus of a different chapter. Those of us who visited Ladd at his office in Burrill Hall witnessed the evolution of this filing system: Later editions (1961, 1973, 1991) were generated from enormous stacks of reprints covering every square inch of flat surface in his office. Remarkably, this filing system was very low in entropy. I recall sitting with Ladd in his office and asking him about a specific paper. Without hesitation he went straight to the appropriate stratum in one of the many stacks of reprints and extracted the exact document I wanted to see. This capacity for accumulating the world's literature was paired with an ability to synthesize what it contained. All four editions of *Comparative Animal Physiology* present not only an enormous set of "trees" but also a synthetic view of the "forest" at large. This was Ladd Prosser at his best: learning everything he could and then returning to the community a beautiful synthesis of what to many might seem a bewildering array of unrelated facts. Among the forms of recognition he received for his scholarship was election to the National Academy of Sciences in 1974. He was elected to the American Academy of Arts and Sciences in 1957 and was awarded a Guggenheim fellowship for 1963-1964.

The diversity of interests found in *Comparative Animal Physiology* was a reflection of the breadth of Ladd's research program, which flowed in several productive channels. His studies included major contributions to the following areas: invertebrate neurobiology; the comparative physiology of muscle, especially the electrical activity and rhythmicity of smooth muscle; temperature physiology, notably the phenotypic plasticity that marks acclimation to different

temperatures; and the general theory of adaptational physiology. Ladd published more than 150 original papers and wrote more than 50 synthetic reviews in these fields. Ladd's 1986 volume, *Adaptational Physiology: Molecules to Organisms*, represented his effort to provide an overview of physiology that vertically integrated information from the ecological to the molecular level. This grand synthesis was the publication that Ladd was proudest of in his huge corpus of work.

In my own area of specialization, thermal physiology, the publications that Ladd wrote with graduate student and postdoctoral colleagues like Andrew Cossins, Jeff Hazel, and Bruce Sidell are landmark papers that helped to define the field. His lab truly was the epicenter of the study of thermal acclimation, and much current work on the molecular details of this process can trace its origins to the questions and publications that originated in Ladd's laboratory at the University of Illinois.

The contributions that Ladd made to physiology include extensive service as an editor of leading journals. He served as editor of *Physiological Zoology* (now *Physiological and Biochemical Zoology*) from 1976 through 1988, bringing this journal to high ranking within the literature of physiology. He also served on the editorial boards of several other journals, including *The American Journal of Physiology*, *The Journal of Comparative Physiology*, and *Comparative Biochemistry and Physiology*. His broader public service included a large number of committee memberships for the National Science Foundation, National Institutes of Health, and National Research Council of the National Academy of Sciences.

RETIREMENT YEARS

Ladd retired from his faculty position at Illinois in 1975 at age 68. Fortunately for the physiological community, his retirement on paper didn't mean much in terms of what

actually transpired in the laboratory. Ladd maintained an active program for an additional 20 years; his final graduate student, William Seddon, obtained his Ph.D. in 1994. During his retirement, Ladd completed a further edition of *Comparative Animal Physiology*, in 1991, and his synthetic book, *Adaptational Physiology: Molecules to Organisms*, in 1986. He continued to be a stimulating presence at scientific meetings, notably the annual meeting of the American Society of Zoologists (renamed the Society for Integrative and Comparative Biology), for which he served as president in 1961. Ladd's withdrawal from laboratory work was necessitated in 1997 when he fractured a hip. Nonetheless, he remained a voracious consumer of the scientific literature, continuing to exchange ideas with colleagues during their visits or through the mail. I received letters from Ladd into his nineties, asking me about this and that, what I thought of a new idea he'd had, and so forth. Ladd's enthusiasm for life was never lost, even with the death in 1998 of his wife, Hazel.

We can be grateful that Ladd's spirit and energy enabled him to complete his autobiographical sketch, which saw publication in 2001. From his own words found in this volume we come to better understand what accounts for his drive, his level of achievement, and his pleasure from the study of nature. In his "Epilogue and Credo" Ladd summarizes his philosophy of life for the congregation of the Unitarian Church that he and Hazel were members of for many years. Ladd emphasized that his atheism is paired with a love of the natural world and a desire to better understand humankind's place in the universe. This deeply humanistic man stated that "evolution is not a theory but a proven fact. Humankind is part of the continually evolving and beautiful web of life. My goal has long been to develop a unified philosophy." The broad comparative focus of Ladd's science can be appreciated in part as an attempt to place our species

into its proper evolutionary context. His pleasure in studying evolution reflects Charles Darwin's belief that there is indeed "grandeur in this view of life." The view of life that Ladd presented to us taught us enormous amounts about physiological evolution and about the human qualities that most ensure the enjoyable and productive exploration of nature's marvelous diversity.

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