W. Maxwell Cowan 1931–2002

Thomas Jessell and Eric Kandel

Max Cowan, one of the founders of modern neural science, died on June 30, 2002. In the course of his long career, Max had a major influence on the scientific scene, both through his research contributions to the fields of neuroanatomy and developmental neurobiology and through his later role as a leader of the national scientific enterprise.

Max was born in Johannesburg, South Africa, and pursued his undergraduate training in anatomy at the University of the Witwatersrand. Then in 1953, at the invitation of the renowned anatomist Wilfrid Le Gros Clark, Max arrived at Oxford University, where he obtained his M.D. and D.Phil degrees.

From the beginning of his career, Max's research was distinguished by his skilled use of anatomy to address physiologically relevant questions. In the early 1950s, in influential experiments with Tom Powell, Max studied the striatal connections of the intralaminar nuclei of the thalamus. This interest led to a now-classic series of studies on centrifugal fibers in the visual system of the pigeon. He was also among the first to explore the potential of strychnine-evoked responses as a way of tracing cortical networks, during a brief period with William Cobb and Michael Wright at the Institute of Neurology in London. In further work with Powell and Ray Guillery, Max applied retrograde degeneration techniques to map the connections of the thalamus and hypothalamus.

In the mid-1960s, Max left Oxford for the US, eventually settling at Washington University in St. Louis. By this time, Max had acquired his longstanding interest in the development of better methods for tracing patterns of anatomical connections, focusing initially on the clever application of biochemistry as an adjunct to more traditional methods. With David Gottlieb, for example, he followed up on Bernice Grafstein's early use of labeled amino acids to study axonal transport. Max saw this as an opportunity to develop a systematic radiographic method for mapping axonal connections in the CNS, a method that soon became widely used.

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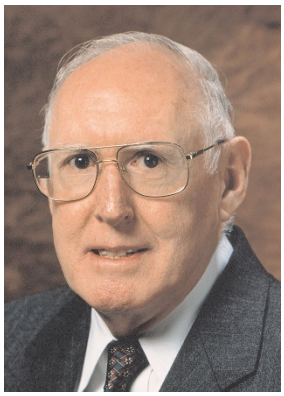

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From the 1970s, with Gary Banker, he also pioneered the development of hippocampal cell cultures, which have subsequently proved invaluable for studying the development and plasticity of central synapses.

In the years that followed, Max helped to focus modern anatomical methods on some of the classic questions of neural development. Building on the work of Viktor Hamburger and Rita Levi-Montalcini, Max documented the generality of cell death in the developing nervous system. Strikingly, Max's studies also revealed that the development of connections in the central nervous system is accompanied by the selective pruning of axons and elimination of synapses. With Dennis O'Leary, for example, he showed that cortical neurons with callosal projections acquire their final patterns of connectivity through the selective elimination of axonal collaterals during early postnatal development.

These two phenomena—cell death and the elimination of neuronal processes—became major themes of Cowan's later work, as he went on to show that these 'regressive' events are likely to result from the deprivation of neurotrophic factors. In this way, he introduced a 'Cowanian' model of brain development that provided the cellular foundation for understanding the role of neurotrophic factors. His work helped to explain, for example, many of the defects in brain development that were subsequently observed in knockout mice lacking the neurotrophins BDNF or NT-3. The perspective that Max introduced also profoundly influenced our understanding of visual cortex development. Many later studies, notably by Lamberto Maffei, Larry Katz and Carla Shatz, have provided persuasive evidence that the retraction of collaterals and the segregation of ocular dominance columns are controlled by neurotrophic factors.

In the course of his long career, Max also trained some of the outstanding anatomists and developmental neurobiologists of our time, including Ray Guillery, Ted Jones, Geoff Raismann, Jenny LaVail, David Gottlieb, Larry Swanson, Cliff Saper, Gary Banker, Dennis O'Leary, David Amaral and Chiko Asanuma. For his many accomplishments, Max was elected to the U.S. National Academy of Science in 1981, and to the Royal Society of London in 1982.

These contributions, which helped revitalize both neuroanatomy and neural development, would constitute a full career for most people. But the remarkable thing about Max Cowan was that, in addition to his eminence as a researcher, he provided national leadership for science in many other capacities. He was president of the Society for Neuroscience from 1977 to 1978. He was the founding editor of both the *Journal of Neuroscience* and the *Annual Review of Neuroscience*. From 1968 to 1980, he was chairman of the Department of Anatomy (later Anatomy and Neurobiology) at Washington University in St. Louis, and from 1982 to 1986, he was the vice-president of the Salk Institute, where he established a lasting tradition of excellence in developmental and systems neuroscience.

Finally, from 1987 to 2000, Max was vice-president and chief scientific officer of the Howard Hughes Medical Institute. In this brief appreciation, it is impossible to document the full extent of Max's accomplishments while at the Institute. He recruited outstanding talent in all areas of science. But beyond this, he created an environment in which people were encouraged to embark on bold and innovative experiments. With great prescience, Max anticipated future developments in all fields of modern biology, and by promoting these developments, left a tangible mark on such diverse areas as structural biology, cellular imaging, molecular neurobiology and, most recently, computational and systems neuroscience.

Very few people are able to combine a productive research career with an effective administrative role at the national level. Max was one of these few, and his legacy in each of the areas that were fortunate enough to have attracted his interest is substantial and memorable.