the JAK-STAT, mitogen-activated protein (MAP) kinase, and Ca^{2+}-calcineurin pathways. Finally, if BOB and its forthcoming kinase are all that there is to the B cell specificity of immunoglobulin production, then why are the immunoglobulin genes not expressed in activated T cells? We are left with an exciting advance but have confronted the well-known paradox: Transcription factors and the signaling pathways that control them are seldom—maybe never—as specifically expressed as the genes they control. One is tempted to suggest that we don't yet know all the players, or even to revert to that last refuge of scoundrels—chromatin.

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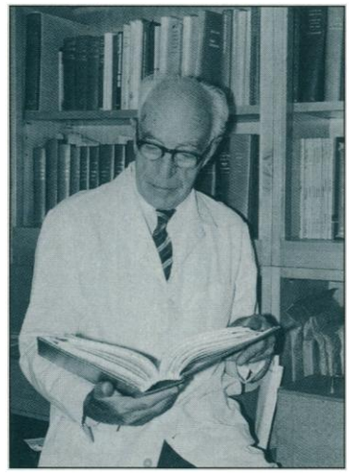
RETROSPECTIVE

John C. Eccles (1903–1997)

Roger A. Nicoll

On 2 May 1997, the neuroscience community lost one of its most influential leaders. Eccles is best known for his work in which he demonstrated that synapses in the brain release chemicals that can excite or inhibit the postsynaptic cell. For this work, he shared the 1963 Nobel Prize with Alan Hodgkin and Andrew Huxley.



Eccles graduated from Melbourne University and attended Oxford University as a Rhodes Scholar, studying under Sir Charles Sherrington. In 1937, he returned to Australia as head of the Kanamatsu Institute of Pathology in Sydney. He moved to New Zealand in 1944 as Professor of Physiology at the University of Otago, and then in 1951 came back to Australia to the National University in Canberra. In 1966, as the mandatory retirement age approached, he moved to the United States, first to Chicago and then to the State University of New York at Buffalo. In 1975 he retired to Switzerland where he lived until his death.

Although best known for his work in the early 1950s on excitatory and inhibitory synapses, for decades before and after this period he dominated the field of neuroscience, touching virtually every aspect of the field. Acetylcholine and Renshaw cells, GABA and presynaptic inhibition, trophic influence of motor nerves on muscle, initial segment and action potential initiation, dendritic action potentials, kinetics of transmitter diffusion in the synaptic cleft, synaptic plasticity, basket cells and inhibition, inhibitory rebound and thalamic oscillations, physiological characterization of cerebellar cortical circuits—these are just a few of his contributions. Each one opened up entire disciplines that are still actively investigated.

But Eccles's most important contribution was his ability to reduce complex problems to simple and exciting concepts. Although his hunger for data was insatiable, he was always after the general principle. This gift is well documented in two of his books, "*The Physiology of Nerve Cells*" and "*The Physiology of Synapses*." These books, which I discovered during my first year in medical school, opened up an entirely new and fascinating world. The message was quite simple: Although the brain is undoubtedly the most complex machine imaginable, one could begin to understand it by studying the individual building blocks, that is, neurons. The neuroanatomist Cajal had also fervently maintained this view throughout his life, but what was so provocative about Eccles's books was that he described how one could, with the aid of microelectrodes, eavesdrop on the ongoing private synaptic communication in a single cell buried deep in the brain. It was now possible to take the beautiful, but static, cellular architecture of Cajal and bring it to life.

From 1973 to his retirement in 1975, I had the privilege of working with Eccles and was able to experience firsthand this larger-than-life character with his childlike curiosity, boundless energy, and extreme tenacity. He, at the age of 72, participated in every experiment (surgery and recording), each of which typically lasted late into the night. The speed and precision with which Eccles performed a spinal laminectomy were breathtaking. I have never encountered anyone so completely consumed by neuroscience, and to this day I and many others remain under his spell. Consequently, it is frustrating that so much of what Eccles contributed seems to be taken for granted. But perhaps this is the way it should be: The really important contributions quickly become second nature to us.

Two of Eccles's most distinguishing traits—his need to understand results in their broadest possible context and his tenacity—were very much in evidence during his retirement. He wrote extensively on the mind-brain problem, vehemently rejecting the materialist view of the mind. Regardless of one's own view on this topic, one had to admire the relentlessness with which he pursued his ideas. As with the scientific period of his life he was a tireless warrior. It is important that his philosophical views, which have few advocates among neuroscientists, not diminish the impact that his extraordinary contributions have had in shaping our understanding of the brain.

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