Murdoch Mitchison 1922–2011

J. M. Mitchison FRS, known to most as Murdoch, Professor of Zoology at the University of Edinburgh from 1963 to 1988, died in Edinburgh on 17 March 2011 aged 88 years. Murdoch was a scientist who marched to the beat of a different drum. Driven by a powerful and individual curiosity into how cells worked, he took little notice of what was current and fashionable, working only on what he judged to be important and interesting. As a consequence he was ahead of his time and was a founder of two fields of research: the development of fission yeast as a model for cell biology and of modern research into the cell cycle. His recognition that yeasts were good models for eukaryotic cell biology predated the subsequent explosion in yeast cell biology and his focus on the cell cycle helped rescue this area from a forgotten backwater, laying the foundations for the advances in understanding cell cycle control that occurred in the decades that followed.

Murdoch came from a formidable academic and political family background. Born in 1922 in Oxford, his grandfather was the physiologist J. S. Haldane, his father Dick Mitchison was a Labour member of Parliament, his mother Naomi Mitchison was a prolific novelist, and his uncle J. B. Haldane was both a Marxist and a world-famous geneticist. His two brothers, Denis and Avrion, are also distinguished biologists, and the production of this trio of large scientific personalities led his mother to quip, so Murdoch told me, that "she was the only mother to have given birth to a third of a ton of Biology Professors". After school in Oxford and Winchester, and University at Cambridge, he joined Army Operational Research in 1941 and was engaged in the Italian campaign during the Second World War. He then returned to Cambridge, finishing his PhD in 1951, before moving to Edinburgh in 1953 where he worked for the rest of his life. He married in 1947 and his wife Rowy was an eminent Scottish historian.

At Cambridge he was present at the birth of molecular biology, co-publishing with Max Perutz and meeting Jim Watson who later dedicated his book *The Double Helix* to Murdoch's mother Naomi. But cell biology was Murdoch's research passion. His early work with Michael Swann was on the cleavage of sea urchin eggs and erythrocyte membranes. Murdoch liked improving microscopes and techniques, and developed an apparatus to measure membrane stiffness, showing there were cyclic changes in surface stiffness during the cell cycle of the sea urchin embryo, a phenomenon later confirmed in amphibian eggs. In the mid-1950s he shifted fields to investigate how cells grow during the cell cycle. He was attracted to fission yeast because it grows only in length during the cell cycle. This was an insightful choice of organism because a cell could be positioned in its cell cycle simply by its length. This is how fission yeast cell biology started. He went on to develop methods to prepare synchronous populations of cells by selecting small cells at the beginning of the cell cycle using gradient sedimentation centrifugation and elutriation, experimental advances which made fission yeast an organism of choice for studies of the cell cycle.

Working mostly with his long-term experimental collaborator, Jim Creanor, and later with Bela Novak, he painstakingly investigated the patterns of increase for many components and processes during the cell cycle. In most cases they showed that the patterns were periodic rather than exponential, often with linear patterns of increase and rate changes. These experiments addressed the important issue of what limits growth. Murdoch's work defined this problem and we have yet to resolve what it means.

Photo courtesy of Neil Mitchison

His second major contribution was to reawaken interest in the cell cycle. The 1971 book *The Biology of the Cell Cycle* had major impact on researchers of the time. He critically reviewed the cell cycle field putting great emphasis on experimental data. Two concepts were particularly important. The first was the distinction he made between the DNA-division cycle, made up of S-phase mitosis and cell division, and the growth cycle, consisting of increases in other cellular components. He argued that progression through the DNA-division cycle in growing cells was dependent on cell growth. This concept had a significant role in developing rate-limiting cell cycle control models. The second concept was that the events of the DNA-division cycle were causally dependent, an early forerunner of checkpoint controls, and that the timing of these events could be determined either by causal dependencies or by master timing mechanisms. Again this had considerable influence on later developments in the field of cell cycle control.

The Biology of the Cell Cycle certainly influenced me and I decided to join his laboratory after my PhD. My first meeting with him was one snowy winter's day in the Zoology Department at Edinburgh. I was a 3rd year PhD student working in a small new university and had published nothing, but he agreed to my request to see him and spent the entire day talking to me about what I might do in his laboratory. What followed was a highly stimulating 7 years under his tutelage. Peter Fantes and Kim Nasmyth came to Edinburgh in the next 2 years and together we began combining genetics and cell biology to better understand the cell cycle and its control. Murdoch was crucial for this. Every couple of days he would pull me into his office, and puffing endlessly on his pipe, discuss the latest experiments and what he was thinking about. These discussions, although they could go on for hours, circling topics, departing on tangents, and becoming blocked in cul-de-sacs, were frequently stimulating, often provocative, and always driven by his passion of wanting to know answers just because he wanted to know, rather than in pursuit of publishing papers. He would always return to the biology, arguing that without good biology the molecular mechanisms were of limited value. Then there was his generosity. He did not put his name on any of the papers I published during those 7 years because he judged he had not been sufficiently involved in the work despite the many hours he had spent discussing what I had done.

Murdoch was responsible for me starting to work on the cell cycle and remained in close contact after I left his laboratory. I met him for the last time with Peter Fantes a few months ago and his enthusiasm for discussion was unabated. Murdoch showed us the way and he will be much missed.

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