Obituary

Professor Bernard L. Ginsborg B.Sc., Ph.D., D.Sc., FRSE (1925-2018)

Professor Bernard L. Ginsborg was Head of the Department of Pharmacology at the University of Edinburgh. He graduated from the University of Reading with a general degree in 1945, an Honours Degree in Physics in 1948, and in 1953 was awarded a Ph.D. in Physics by the University of Reading for his work on visual optics. Bernard was elected Fellow of the Royal Society of Edinburgh in 1971, and was awarded a D.Sc. by the University of London for his subsequent contributions on "ion movements in junctional transmission".

Although he was a committed atheist, Bernard's Jewish identity remained important to him throughout his life. This was perhaps because he retained an open mind in all things, highlighted by his suggestion that science - in the form of the Edinburgh Multi-Access Computer, with its multiple terminals - might prove him wrong. This open mind and sense of adventure, which he never lost, informed his scientific work, interests in music (particularly Mahler and Wolf), literature, and his life as a whole. There are few lay enthusiasts who would, for example, learn both Russian and French in order to read "the classics" in the languages in which they were meant to be read.

Bernard was born on the 22nd of January 1925, the youngest child of Henry Ginsborg and Mala Rebbe, who fled to England from Riga (Latvia) and Kovno (Lithuania) in 1914, "between the revolutions". Henry worked as a "Wharfinger" (wharf labourer) in east London, then as a supervisor in a toy factory. Bernard won a scholarship to Owen's Boys School, where, after being evacuated to Bedford during World War II. The School encouraged him to apply for Oxford or Cambridge but he resisted; his family was poor, and he did not think he would enjoy the life of a student there. He opted instead to attend Reading University to study Physics, where he met his future wife, Andy (Andrina; who became one of the first Clinical Child Psychologists to practice in Scotland, at the Royal Hospital for Sick Children). He completed his first, general degree in 1945 and applied for a commission in the RAF, but was rejected. Instead he made his contribution by co-developing the first humidity proof cigarette packaging, "for our boys" in South East Asia; with life expectancy so short and the dangers of smoking yet to be realised, the brief moments of escape afforded to the troops were no doubt appreciated. After the end of World War II, Bernard went on to take a B.Sc. (Hons.) in Physics, which he completed in 1948. At this point he was committed to studying for a Ph.D., but actively sought a subject that was of no use to "man or beast", having seen the devastation wrought by the nuclear bombs dropped on Hiroshima and Nagasaki. Bernard found one, under the supervision of R. W. Ditchburn.

Ditchburn had noted with interest, that if one looked with one eye down different lengths of hosepipe, at a certain length one's capacity for vision was always lost; a test soon to be repeated by Grandparent and Grandchild on garden benches across the world. Bernard received his PhD in 1953, a year after his first two papers on the subject of "flickering eye movements" were published by Nature Magazine; the greater detail of these investigations being published elsewhere (Journal of Physiology in 1953), as was the norm at that time. However, it is interesting to note an earlier publication in 1951, regarding the deposition of rubidium on Perspex. This points to a remarkable fact, that Bernard had designed a reflective "contact lens" to allow him to obtain measurements from willing subjects – himself. Aided by this lens, a jaw clamp designed by a dog dentist he met at a dinner party, a cine (video) camera, a restraining chair and user-operated light source, he discovered tiny involuntary eye movements that he named "flicks", which are important to the maintenance of visual perception during fixation and were later renamed microsaccades (by some bright spark). This work overturned the Polychromatic Theory of vision. Studies on the contribution of these involuntary eye movements to visual perception are ongoing today. Bernard moved on, however, captivated by the work of Katz, Fatt and colleagues in the Biophysics Department of University College London, regarding the new biophysics of neuromuscular transmission. He approached Katz for a job, who asked if he had a degree in Physiology. Bernard said he did not, so Katz suggested he go off and study for one. Bernard did so, and returned a year later, during which time he got the impression that Katz had read his CV.

Bernard's initial contribution in the field of neurotransmission was with Liam Burke. They were the first to investigate the electrical activity of slow muscle fibres, which represent a proportion of most skeletal muscles and aid long-endurance activities. Burke and Ginsborg (1956) demonstrated that slow fibres are distinct from fast twitch skeletal muscles in that they are electrically inexcitable, and that this was in part due to 'delayed rectification' conferred by increases membrane permeability to potassium ions. Thereafter Bernard collaborated with Paul Fatt on the excitability of crustacean muscle fibres. This investigation was founded on an earlier paper by Fatt and Katz (1953), reporting the unexpected finding that the sodium hypothesis of Hodgkin and Huxley to explain excitability of nerve axons did not apply in crustacean muscle fibres: "The mechanism of the action potential, and the species of ions involved in the movement of charge across the membrane remain a puzzling problem". In 1958 Fatt and Bernard solved this puzzle, when they discovered

that electrical stimulation of the crustacean muscle membrane elicited a calcium action potential. This was a turning point, not simply for demonstrating the existence of voltage-gated calcium currents, but because it showed that the calcium ions entering excitable cells through these channels caused increases in intracellular calcium concentration large enough to influence events such as contraction and secretion. As Otto Loewi once said, to a cell "calcium is everything".

The aforementioned contributions alone hint at the fact that by any measure Bernard was an outstanding scientist, thorough, persistent and with a keen eye for unexpected details. It has been said, quite rightly, that he "only rarely allowed his vast breadth of knowledge to break the surface, and only the most pompous ever drew the sharpness of his tongue". His modest enthusiasm encouraged and inspired students, post-docs and collaborators alike. It was also reflected in the fact that he only ever accepted co-authorship when he had made a significant contribution, leaving the more independent, unsuspecting disciple disappointed.

In 1957 he was recruited to the scientific staff of the Medical Research Council, National Institute at Mill Hill by Walter (later Lord) Perry, who he followed to Edinburgh as a member of the external staff of the MRC (1958-62). In 1962 he was appointed to a Lectureship, then a Readership (1964) and Personal Chair (1976). He then succeeded Eric Horton as Head of the Department of Pharmacology. During 1967 he had elaborated on his considerations regarding "Ion movements in junctional transmission" in Pharmacological Reviews, foreseeing the dramatic changes in our understanding of ion channels and their influence on system control that occurred from the 1980s onwards; notably, his modelling of cellular activities by equivalent circuit was famously adopted by Kandel for his textbooks of neuroscience. This informed the equally broad range of investigations Bernard published (several in Nature) during the rest of his career, from determining the multiple endplate regions of avian skeletal muscle, synaptic transmission in amphibian sympathetic ganglia, presynaptic inhibition by ATP at the mammalian neuromuscular junction, and latterly dopaminergic transmission at insect salivary gland cells. As ever, the departure to insect salivary gland cells was with purpose, as they represented a different system operated through "slow" (G-protein coupled) receptors, but, much like the neuromuscular junction, one that was accessible to techniques of the day. Critical biophysical analysis identified a delay between stimulus and response that suggested a role for second messengers in the mobilisation of intracellular calcium stores and the control of secretion; presenting others with a model system for investigations that led to the discovery of the first calcium mobilising messenger, IP_3. Bernard's studies culminated in a description of store-depletion activated calcium entry, Ginsborg, Mitchell and House (1980) reporting in *The Journal of Physiology* that dopamine stimulated: "the influx of calcium into the cytosol from a store that can only be replenished from the exterior" (extracellular fluid). It is notable that this field of investigation accelerated after his retirement, with little attention given to this seminal paper.

All who worked with Bernard found him challenging, enlightening and great fun. As his great friend and colleague Randall House put it "if Bernard had chosen a musical career instead of science he would have been a virtuoso". It is apt that he died shortly after the 250th anniversary of the founding of the Chair of Materia Medica (Pharmacology) by the University of Edinburgh and with it establishing the discipline of Pharmacology, and on the 100th anniversary of the year in which the first pure scientist was appointed to this Chair. Bernard remains an inspiration to those who knew him, while his papers stand as models of scientific endeavour and writing. Many are given avenues to follow, all too few are pioneers.

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