

# Guest Editorial

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## REMEMBERING SIR BERNARD KATZ (1911-2003)



True science recognizes no boundaries and it is best exemplified by the life of Sir Bernard Katz, an ideal role model for a generation of physiologists and pharmacologists and who was instrumental in the “Quantum” jump in the knowledge of synaptic physiology.

Max Katz, the father of Bernard Katz, was a Jew fur trader in Tsarist Russia but had left Russia in 1904 and settled in Germany, where he met and married Eugenie Rabinowitz, a woman of Polish origin. Bernard Katz was born in Leipzig, Germany on 26th March 1911. As a child till 6 years, Bernard Katz was a citizen of Russia but became stateless because of the Russian Revolution and later, ironically his statelessness made it easy for him to escape from Nazi oppression and leave Germany inspite of the fact that he was a Jew and Hitler was at the helm when Bernard Katz left Germany.

Katz's early schooling was at Konig Albert Gymnasium in Leipzig and the atmosphere was ‘completely unorthodox and liberal’ as he himself has put it and ‘he chose to learn Latin and Greek rather than more mathematical options as it gave him more time to play chess in the cafes of Leipzig’. Despite this, and inspite of having had his share of anti-Semitic experiences, he did well at school and went on to study Medicine at the University of Leipzig in 1929. After finishing his pre-clinical examination in 1931, he combined his undergraduate work with part-time physiological research under the guidance of Martin Gildemeister. His first work on muscle stretch and impedance resulted in two research papers and also in getting him Siegfried Garten prize and helped him secure M.D. degree.

After completing his medical degree in 1934, he continued to work in Leipzig hospital by which time he had read about A V. Hill and had realized that his research work had similarities with that of A. V. Hill and decided to leave Germany and work under him at the University College of London (UCL). At the beginning of February 1935, Katz left Germany and reached the doors of Department of Physiology, UCL, in a few days after travelling by train and ferry and ultimately reached his destination, Prof. A. V. Hill with just 4 pounds in his pocket along with a recommendation letter from Gildemeister.

A. V. Hill was a great man, not only as a scientist (he had already been honoured with Nobel Prize in 1922), but also as a good human being and had a great influence on Katz for the rest of his life. As Bernard Katz puts it, "It was an outstanding piece of good luck to have been taken on as an apprentice to A. V. Hill, it was the decisive influence on my life and career. He was the person from whom I have learned more than anyone else, about science and about human conduct. A. V. Hill was the most naturally upright man I have ever known. To be associated with a man of his stature at a formative period of one's life is indeed a great gift of fortune".

Katz worked under A. V. Hill from 1935 to 1939 and received his Ph.D. in 1938. In 1939, a month before the start of the Second World War, he left to Australia to work with John Eccles, another renowned neurophysiologist, at the Sydney Hospital as a Carnegie Research Fellow, during which time he worked on synaptic physiology and neuro-muscular transmission. In 1941, he became a naturalized British Citizen and soon after served as a radar officer at New Guinea in the Royal Australian Air Force till the end of the war. Meanwhile, he met Marguerite Penly (Rita) of Cremore, New Southwales who incidentally was not a Jew and they got married immediately after the war. A month after the wedding, in 1946, Katz returned to UCL as Assistant Director of Research in Biophysics and Henry Head Fellow of the Royal Society.

In the immediate postwar period, although based at UCL, Katz spent most of his time working at Cambridge and at marine laboratory Plymouth with Alan

Hodgkin and Andrew Huxley. They were then engaged in the research that led to the discovery that the overshoot of action potential results from an influx of Sodium ions. Along with this discovery, Katz's other early work included the discovery of the phenomenon of inward ('anomalous') rectification. Bernard Katz worked as a Reader in Physiology at UCL from 1950 to 1951 and later succeeded his mentor A. V. Hill as the Professor of Biophysics and headed the department of outstanding distinction till 1978.

By 1950s, unraveling the mystery of the regulation and transmission of nerve impulses and neuro-muscular transmission had become the key areas of research. Two major extrinsic factors were driving the research in this direction. One was the need to understand the effects of organocholine and organophosphorous compounds, the basis of nerve gases and the other was the possibility that the detailed understanding of the basis of generation and transmission of nerve impulse and neuro-muscular transmission would help in medicine like the treatment of some of the diseases of the nervous system. Hence the choice made by Katz in the immediate postwar years was influenced by these factors as well as by his mentor A. V. Hill, who was already involved in this field of study and was also a wartime Cabinet Scientific Adviser under Winston Churchill and there was *an urgent felt need* to solve these questions. Uppermost among the mysteries of neural signal transmission was how the discrete electrical impulses of a nerve fiber cross the large gap observed at each nerve junction with its target cell and bring about response quickly and faithfully. Dale had already

shown that the transmission was not electrical but chemical and that acetylcholine was involved at the neuromuscular junction. Katz unraveled the detailed biochemistry of the dynamic cycle and also the central role of acetylcholine and its key enzymes and went on to show that even when a nerve is inactive, the acetylcholine cycle at the junction continues transmitting tiny 'bleeps'. His major discovery was that this resting signal does not depend on individual molecules but it depends on the release of small packets of transmitter substance, which cross the junction and bring about an electrical response in the muscle fiber. This is brought about by the action of acetylcholine acting on the 'receptors' at the end plate, opening 'aqueous pores' in the muscle membrane leading to the influx of cations and thus bringing about the electrical response. Thus, Bernard Katz spoke on 12 December 1970, while receiving the Nobel Prize for this seminal work, "Some 20 years ago, using the method of intracellular recording, Paul Fatt and I came across something quite unexpected. In the absence of any form of stimulation, the end-plate region of the muscle fiber is not completely at rest, but displays electric activity in the form of discrete, randomly recurring 'miniature' end-plate potentials. Numerous experiments have shown that each miniature end-plate potential arises from the synchronous impact of a large multi-molecular quantum of acetylcholine spontaneously discharged by the adjacent nerve terminal".

Katz went on to show that the single 'packet' of molecules, characteristic of the resting signal, is the minimum amount that can produce a corresponding signal in the

receiving cell. As the signal strength rises through increased frequency of impulses, this is mirrored rapidly by a stepwise increase in the release of acetylcholine packets across the junction. Katz proved the first perception of neural function at the molecular interaction level, the basis of all later understanding of neural function at the molecular level. He, with his fellow colleagues at UCL established all the important features of synaptic transmission, like the role of calcium in vesicular release, the enzyme cycles involved in the production and inactivation of transmitter substances, the effects of transmitters on the post synaptic membrane which was the basis of later discovery of 'ion channels', and also that all these processes are highly vulnerable to disruption. The influence of his work is inestimable, not only in physiology, but also in pharmacology where his suggestions of a mechanism for partial agonism and the first rigorous demonstration that d-tubocurarine was a competitive antagonist became the building blocks for future extensive research in pharmacology.

Bernard Katz's perception of a problem and his uncanny instinct for separating the important from the trivial were legendary. Characteristically he would approach a fundamental problem that appeared to be settled and by tackling the question in a new manner, he would open up fields that had never been dreamt of. His realization of the importance of 'small and unpromising spontaneous 'bleeps' recorded by the instrument at the neuromuscular junction' eventually led to the discovery of quantal transmitter release at the neuro-muscular junction. Similarly, the importance he attached to the 'apparent

increase in the noisiness of the recorded signal when acetylcholine was present' and his subsequent work on this noise analysis gave, although indirect, information about how single ion channels would probably behave. This led to further discussions as to whether recording from single channels can be made and ultimately resulting in the actual recording from the single channels, not much later, by Bert Sakmann (with Erwin Neher), who was a post doctoral fellow at UCL during that time and was a part of this discussion. This work was also honoured with the Nobel Prize in 1991. Along with this, Katz's genius was to reveal new dimensions of a seemingly simple problem on which others would work and build on subsequently. Thus his work on chemical transmission serves today as the stepping stone for studies on memory, work on molecules in nerve cell membranes that are sensitive to chemicals is the basis of important concepts in molecular biology and work on release of transmitter substances has revealed mechanisms of secretion not just by nerve endings, but also by glands.

Katz used simple and elegant techniques of experimentation which was matched by an equally elegant and fine style of writing and lecturing. At the same time he set very high standards and was very passionate about science and hence could not tolerate sloppy thinking or error. He was always willing to discuss with the most junior of the students and offer valuable advice about their works. His Ph.D. students (though only five) went on to do eminent work and his lab was a Mecca for many post doctoral fellows and the list of them is a Who's Who of distinguished professors throughout

the world. He led the department with outstanding distinction till 1978 when he retired as professor but continued as a Honorary Research Fellow till his death on 20 April 2003 actively contributing to the science till the last day in true sense.

During his illustrious career, he was justly awarded with many honours, most notable of them being Fellow of Royal Society (1952), Copley Medal of Royal Society (1967), Knighthood (1969) and to top them all, he was awarded with the Nobel Prize in Physiology or Medicine in 1970, jointly with Ulf von Euler of Sweden and Julius Axelrod of USA. Thus Bernard Katz who born in Germany as a son of a Polish mother, and a Jewish father from Russia, and who had a taste of Nazi oppression, but became a naturalized British citizen, and married a non Jew from Australia became instrumental in the "quantum" jump in the knowledge of synaptic physiology contributing immensely to the understanding of some of the basic principles which were later worked on by many other scientists all over the world, reiterating the fact that science has no boundaries.

Bernard Katz remembered his mentor A. V. Hill throughout his life and truly learnt from the great teacher. In the preamble to his inaugural lecture given in 1952 when he became the professor, Katz expressed his gratitude to A. V. Hill 'for all I have learnt, not only as a pupil of a great master of experimental research, but by having served my apprenticeship with a man who never, under any circumstances, allows the deceptive counsels of human

vanity to enter into your argument-with a man whose one inflexible purpose has always been the pursuit and acknowledgement of truth'. These same words describe equally well Bernard Katz, who with his love for truth, modesty and high ideals coupled with detestation for

showmanship and dishonesty, was and continues to be a role model for many even at this time, more so now where there is a paucity of such great people. Sir Bernard Katz passed away on 20th April 2003 and it is never too late to learn from and follow such noble souls.

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University of Leipzig : <http://www.uni-leipzig.de/english/index.html>

University of College London : <http://www.ucl.ac.uk>

The Nobel Prize in Physiology or Medicine 1970 : <http://www.nobel.se/medicine/laureates/1970/index.html>

Karolinska Institute : [http://info.ki.se/index\\_en.html](http://info.ki.se/index_en.html)

The Royal Society : <http://www.royalsoc.ac.uk/>

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## CORRIGENDUM

The Editorial Office regrets to inform the readers and all concern parties that the article entitled, "Effect of Occupational Noise on the Nocturnal Sleep Architecture of Healthy Subjects" By B. Gitanjali and R. Dhamodharan published in IJPP 47(4): 2003; 415-422 has been inadvertently reprinted in IJPP 48(1): 2004; 65-72. The latter should be considered null and void.