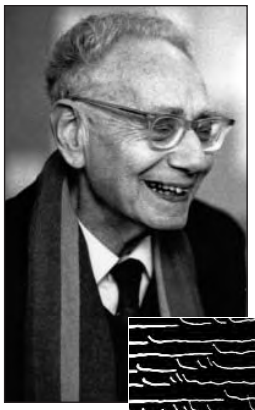
# "My Little Spontaneous Blips"

John Heuser

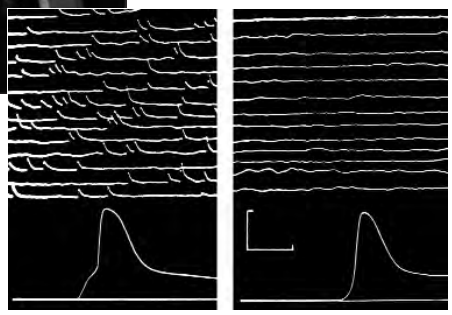
So wrote Sir Bernard Katz (*1*), of the observations that eventually led to his being awarded the Nobel Prize for discovering the mechanism of neural secretion. This "father" of the fields of biophysics and neuroscience died of natural causes on 20 April 2003, at the ripe old age of 92. He continued to live and work in London until the end, although with diminishing enthusiasm after the death 4 years ago of his beloved wife of 54 years, Rita.



Katz's legacy is immense—from the solid scientific foundation he and his collaborators established in the field of neuroscience, to the extraordinary number of budding scientists he "sired" by welcoming them into his laboratory as postdocs.

Katz was the first person to observe tiny electrical "blips" at the synapse (see the figure), which he termed "miniature endplate potentials" ("endplate" because he was recording from frog muscle, where the postsynaptic element is so named). Correlating these electrical blips with the tiny packages of membrane ("vesicles") that had recently been discovered by electron microscopy inside the synapse, Katz realized that his blips couldn't be individual "hits" of single neurotransmitter molecules upon the postsynaptic membrane. He surmised that they must be multimolecular "packets" of nearly uniform size (thus, the term "transmitter quanta") released by discharge of individual synaptic vesicles.

Some years later, Katz and his chief collaborator, Ricardo Miledi, finally realized that by racking up the gain on their electrical amplifiers, they could indeed recognize individual molecular "hits" upon the muscle's postsynaptic "endplate" membrane. However, these molecular hits came so fast and furiously—and were so tiny—that they still appeared as electrical "noise" that could only be resolved into individual events by computer-based Fourier analysis. Working day and night with the only computers available in London in those days—primitive devices that choked the halls of the chemistry department at University College—Katz and Miledi went on to describe these individual molecular "hits" in quantitative terms. In this way, they achieved the first-ever direct "visualization" of a single molecular event—in this case, the conformational change that a synaptic chemoreceptor undergoes when it interacts with its neurotransmitter (acetylcholine, in the case of the nerve-muscle synapse) resulting in opening of a channel or "pore" in the postsynaptic membrane. Individually, these molecular reactions create only minute depolarizations of the muscle, the "noise" that Katz and Miledi saw when they applied acetylcholine experimentally. But during normal synaptic transmission, when hundreds of thousands of acetylcholine molecules are abruptly released by calcium-activated discharge of many hundreds of synaptic vesicles simultaneously, these channel openings act in concert to completely depolarize the muscle and make it contract.



Thus, in one lifetime, Katz (with Miledi and his earlier collaborators, del Castillo, Fatt, and Jenkinson) elucidated the whole mechanism of synaptic transmission—from presynaptic neurosecretion by discharge of transmitter quanta from within the synaptic vesicles populating motor nerve terminals, to postsynaptic chemoreception by the transmitter-induced opening of individual molecular channels or pores covering the muscle endplate membrane.

No department was held in higher esteem in its day than the Biophysics Unit at University College, London, headed by Katz. For nearly 40 years, aspiring young scientists came to this laboratory to work under him and Miledi. Here, they felt that they were in the Mecca of neuroscience, and as such, were being offered a tremendous head start toward becoming the next generation of leading neuroscientists (which many of them did). In this "hothouse" environment, Katz's presence was always gentlemanly; but it was also intense, in terms of his exemplary intellectual and personal influence. Katz personally assigned all projects, oversaw all progress through weekly meetings or "pass-throughs" of each individual's laboratory, and painstakingly reviewed and edited all manuscripts before any of the junior members of his unit submitted their work for publication. Many remember this latter aspect of his influence as the most wonderful of all. Some have even declared that Katz's command of the English language and of scientific expression was totally unsurpassed. This, despite the fact that Katz was German-born and did not emigrate to England until he graduated from medical school, forced into exile by the rise of Nazism.

Katz followed in the footsteps of the great muscle physiologist A. V. Hill, who had spoken out strongly against Nazism and had been instrumental in arranging his escape from Germany (*2*). Katz admired Hill so much probably because both men were (in Katz's own words) "united in their enthusiasm for the possibility of making very accurate measurements on living tissues, with relatively simple technical equipment," and were "fascinated with establishing precise quantitative relations and applying a mathematical theory to the results" (*3*).

Speaking of one particular equation that Katz himself derived and that particularly pleased him (the equation that gave two separate and independent ways of determining the average number, $n$, of quantal packets of neurotransmitter released by each motor nerve impulse), Katz quipped, "You may well ask why I make so much out of such a simple formula. The answer, I suppose, is that being mathematically naïve, I see some beauty in what others with more knowledge and experience may regard as trivial" (*4*).

Katz was blessed by making not one but two major scientific discoveries—discoveries that opened whole new fields in neurobiology. When asked on Japanese TV about what he thought it took to become the outstanding scientist he was, Katz answered humbly: "I cannot give a prescription; but it needs a combination of intelligence, willpower to overcome setbacks, readiness to follow unexpected leads, plus a good mentor and a great deal of luck!" Katz had all of these traits in spades. His proteges have been blessed by his influence personally, and we will all continue to be blessed by Katz's lasting scientific legacy.

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### References and Notes


1. B. Katz, *Creativity Res. J.* **7**, 225 (1994).
2. For a complete description of Hill's great role in science in general and his influence on Katz in particular, see B. Katz, *J. Physiol.* **370**, 1 (1986).
3. Personal letter to the author from Sir Bernard Katz, dated 18 January 1994.
4. B. Katz, in *Neurotransmitter Function*, L. C. Sellin, R. Libelius, S. Thesleff, Eds., vol. 13 of *Fernstrom Foundation Series* (Elsevier, Amsterdam, 1989).
5. P. Fatt, B. Katz, *J. Physiol.* **117**, 109 (1952).


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