OBITUARY

Lawrence C. Katz (1956–2005)

Neuroscientist who helped to make sense of sense.

B. A. RENKIEL

In 1981, just as Larry Katz was beginning his postgraduate career, the Nobel Prize in Physiology or Medicine was awarded to David Hubel and Torsten Wiesel for their pioneering studies of the visual cortex. They had deduced that the vertical columns of neurons in this part of the outer, grey-matter layer of the brain, responsible for processing visual stimuli, are organized into sets — orientation columns and ocular dominance columns — according to their responses to visual stimuli. This discovery came largely through painstaking microelectrode recordings of single neurons, combined with anatomical tracing of connections from eye to brain that revealed a highly organized stripe-like segregation of inputs representing the two eyes in cortical layer 4, the gateway to the cortex.

What was missing from this picture was an understanding of how neuronal connections within the other layers of the cerebral cortex are organized. A cortical column comprises some 10,000 neurons, each making thousands of connections. Aside from hard-won intracellular recording experiments from a handful of single neurons, and beautiful studies that revealed primarily the dendritic morphology of these cortical neurons, little was known about their local axonal branches — the transmitting end of the neuron — let alone about functional synaptic connections. Hubel and Wiesel's work had demonstrated that the columnar organization of the visual cortex could be profoundly perturbed by abnormal visual experience during a critical period of development; but how the cortical columns formed in the first place, or what aspect of altered experience perturbed them, remained mysterious. Answers required new methods of studying the cortical connectivity of several neurons simultaneously, in terms of both anatomy and function.

These were the unresolved questions with which Larry Katz grappled during his tragically short 25-year career, providing many answers and leaving a precious legacy of technological innovation. Katz typified a new breed of scientist, able to combine innovation with a willingness to work on problems, such as those of the wiring of the visual system, that seemed too complex to approach experimentally.

Katz arrived in 1981 at Mark Konishi's laboratory at the California Institute of Technology in Pasadena with a love of neuroethology — the study of brain and behaviour — and with papers on tadpole and fiddler-crab behaviour, written as an undergraduate at the University of Chicago, under his belt. His intention was to study the brain circuits underlying birdsong. Encouraged by Konishi, however, he switched his focus to the mammalian cerebral cortex, devising in his doctoral thesis of 1984 a striking approach for studying subsets of cortical neurons through the long-distance connections they make with other neurons.

The tracing method that Katz invented used fluorescent latex microspheres that permitted the retrogradely labelled neurons not only to be visualized in slices *in vitro*, but to be simultaneously targeted with a microelectrode and injected with dye. This technique, which Katz perfected as a postdoctoral fellow with Torsten Wiesel at the Rockefeller University, New York, is still popular today, generating images that have graced many journal covers. Quite apart from the beauty of the experiments, the method threw wide a door, opened only a crack by conventional methods, that enabled Katz to examine in exquisite detail the development of horizontal connections between neurons, and show how this development could be influenced by experience.

Not content with an anatomical view of the cortex, in the 1990s Katz — now at his own laboratory at Duke University in Durham, North Carolina — pioneered the application of optical imaging of neurons (using fluorescent calcium or voltage indicators) and photostimulation (using caged glutamate) to probe circuit development. He thus provided new views of cortical circuits, discovering the existence of spontaneously active groups of neurons, known as coactive domains, and probing the emergence of functional horizontal connections within cortical layers 2 and 3.

Katz was never afraid to develop or apply new technology when it was needed for the optimal execution of an experiment. For example, many experiments pointed to a need for correlated neural activity during brain development to fine-tune sets of connections in the cortex that underlie ocular dominance and orientation columns. But *in vivo* evidence for correlated spontaneous firing of ensembles of neurons was missing until Katz perfected a method of multi-electrode recording in conscious, behaving animals.

From 1999 until his untimely death from melanoma on 26 November 2005, Katz's science began to come a full circle, as he returned to his original interest in neuroethology. In a marvellous conjunction of the best of technology and the best of neuroscience, Katz marshalled his impressive armamentarium to attack the problem of how olfactory signals are processed in the rodent brain. He used the technique of intrinsic signal imaging to reveal a spatial map of odours among structures in the olfactory bulb known as glomeruli, where the first stage of information processing in olfaction occurs. And, in a 2003 tour de force with collaborators Minmin Luo and Michale Fee, he achieved the extraordinary feat of recording neuronal activity in the accessory olfactory bulb of awake, behaving mice. Studying this pathway, which is parallel to the main olfactory pathway and functions as the 'sexual nose', enabled Katz to reveal for the first time the encoding of responses to pheromones — chemical signals transmitted between members of the same species.

Katz's choices of scientific problems centred throughout his career on the key senses of hearing and language (birdsong), sight and, most recently, smell. He appreciated not only on a scientific level the extreme elegance of the brain circuits that process sensory information, but also on a human level their role in connecting us to each other and permitting us to enjoy the world around us to the full. Larry's joy for living and aesthetics no doubt accounted for his love of the sleek design of the Alpha Romeo cars that he drove for years, and of the speed and soaring freedom of flying an aeroplane. He was also an avid fisherman, and we can imagine him even today with a prize albacore or up to his knees in a rushing stream high up in the wilderness, reeling in a trophy trout. ■

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