# Paul Fatt
# 1924-2014

Faces left to right: Murdoch Ritchie, Paul Fatt and Doug Wilkie in conversation in the old Physiology classroom, UCL 1979. Photo: Martin Rosenberg, with permission of The Physiological Society.

With the death of Paul Fatt on 28th September, we lost one of the founders of modern cellular neuroscience. He ranks among the most distinguished neuroscientists and biophysicists of the twentieth century. Working with Bernard Katz and a number of other exceptional collaborators, notably John Eccles and Bernard Ginsborg, Paul Fatt realized a staggering series of fundamental discoveries on excitatory and inhibitory synaptic transmission, and ion channel function.

The second of three scientifically-minded brothers from Chicago, Paul Fatt received his education in Biochemistry at UC Berkeley on the G.I. Bill after serving with the US Army in WWII. As a young graduate student, he joined UCL's Biophysics Research Unit (later the Biophysics Department) in the summer of 1948. He and Katz decided that they would 'have a go' at using intracellular microelectrodes to examine the endplate potential (EPP). It is no exaggeration to say that the decision opened up a new era in our understanding of synaptic transmission. Together they carried out the first analysis of the endplate potential using intracellular microelectrodes - an experimental *tour de force*. This was the first compelling demonstration that synaptic receptors were chemically gated ion channels.

During the spring of 1950, Fatt and Katz made the chance observation that, when examined on a high recording gain, the endplate region of skeletal muscle was the site of spontaneous ongoing electrical activity. This they ascribed to the discharge of multimolecular 'quanta' of acetylcholine (ACh) from the nerve terminal. In a series of elegant experiments, they demonstrated that these events, dubbed miniature endplate potentials (MEPPs), represented the 'basic coin' of chemical synaptic transmission – and that the full sized EPP triggered by a nerve impulse, represented the superposition of a large number of synchronously occurring MEPPs.

The EPP, and its constituent 'miniatures' became the fundamental model against which transmission at other chemical synapses, including those in the brain, have subsequently been compared.

In the summer of 1952, on completion of his PhD, Fatt left UCL for the Australian National University in Canberra to work with John Eccles, where, working in motoneurons, they identified the ionic mechanism underlying postsynaptic inhibition as arising predominantly from an increased chloride conductance. During this study, Fatt developed the double-barrelled microelectrode technique - two glass barrels fused and twisted together by melting, and then pulled into a fine tip with a diameter less than a micron. One barrel was used to record the synaptic potential changes while the other injected current to alter the ionic composition or preset the membrane potential.

Fatt further identified the different regions on the neuron associated with the electrical components of the spike, recognizing for the first time the ways in which the initial segment and soma dendrite determine the action potential properties of central neurons. He has also been widely credited with the prediction that transmission could be mediated electrically rather than chemically at certain synapses – something confirmed soon after in a classic study by Furshpan & Potter.

Fatt came back to London in 1956 to take up a position in UCL's Biophysics Department where he returned to the more accessible synapses offered by crayfish muscle. Here, he established the general mechanisms underlying postsynaptic inhibition by demonstrating that externally applied GABA and inhibitory nerve impulses both produced postsynaptic chloride conductance increases, mediating the inhibitory current at these synapses. Furthermore, Fatt, together with Bernard Ginsborg, worked on the ionic requirements for action potential generation in crayfish muscle, discovering for the first time the existence of $Ca^{2+}$-mediated action potentials, one of the most important currents present in biological tissues.

In the mid 1960s, Paul Fatt worked with his then wife Gertrude Falk on the membrane system of skeletal muscle using the electrical impedance methods developed by K.S. Cole to understand how skeletal muscle had a membrane capacitance which far exceeded the value predicted from muscle fibre size. Supported by subsequent electron microscopic evidence, they showed that the muscle surface included a connecting internal membrane system, the transverse tubule network, responsible for spreading excitation into the centre of the muscle fiber.

Paul Fatt was part of a remarkable generation of highly talented and practical scientists who returned from WWII and populated Physiology and Biophysics departments. Paul remained at UCL for nearly his entire career - preferring to spend time experimenting himself rather than running a large research group. Even so, he influenced generations of UCL Physiology and Pharmacology students as a result of his annual Biophysics Course - a six week practical course which he ran with Gertrude Falk (and other members of the Biophysics Department). His lectures were admirably unpretentious, utterly engaging, sometimes baffling, but always enjoyable. We recall Paul being asked during a lecture why MEPPs always seemed to appear on the oscilloscope screen in groups if they did indeed occur randomly. Paul's response was typical: he pointed out that if you waited on Tottenham Court Road for the 24 bus (his daily route home to Hampstead) you would notice these also always arrived in twos

or threes. And, like MEPPs, if you plotted the interval between them they fitted an exponential. It not only conveyed his point in a charming way but, to our great amusement as students, suggested London buses were entirely random. Paul's infectious enthusiasm for his subject contributed greatly to the fact that such a high proportion of students taking the course (the authors included) ended up as neuroscientists.

Although Paul never set much store by accolades, his significant contributions were marked by election to the Royal Society in 1969. Paul was never tied by convention and was fiercely liberal in his views. His warm and generous personality and sharp intellect had a formative effect on many of his younger colleagues. And his remarkably large number of landmark discoveries have guaranteed that his name will long remain familiar to seasoned neuroscientists and students alike.

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