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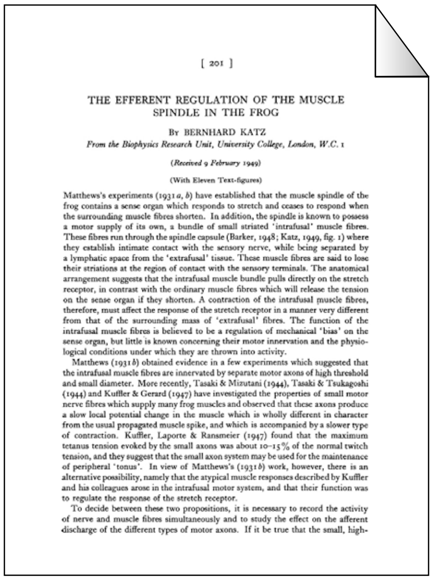
MOTOR INNERVATION OF THE MUSCLE SPINDLE: THE CONTRIBUTION OF BERNHARD KATZ



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THE EFFERENT REGULATION OF THE MUSCLE SPINDLE IN THE FROG

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(With Eleven Text-figures)

Matthews's experiments (1931 *a*, *b*) have established that the muscle spindle of the frog contains a sense organ which responds to stretch and ceases to respond when the surrounding muscle fibres shorten. In addition, the spindle is known to possess a motor supply of its own, a bundle of small striated 'intrafusal' muscle fibres. These fibres run through the spindle capsule (Barker, 1948; Katz, 1949, fig. 1) where they establish intimate contact with the sensory nerve, while being separated by a lymphatic space from the 'extrafusal' tissue. These muscle fibres are said to lose their striations at the region of contact with the sensory terminals. The anatomical arrangement suggests that the intrafusal muscle bundle pulls directly on the stretch receptor, in contrast with the ordinary muscle fibres which will release the tension on the sense organ if they shorten. A contraction of the intrafusal muscle fibres, therefore, must affect the response of the stretch receptor in a manner very different from that of the surrounding mass of 'extrafusal' fibres. The function of the intrafusal muscle fibres is believed to be a regulation of mechanical 'bias' on the sense organ, but little is known concerning their motor innervation and the physiological conditions under which they are thrown into activity.

Matthews (1931 *b*) obtained evidence in a few experiments which suggested that the intrafusal muscle fibres are innervated by separate motor axons of high threshold and small diameter. More recently, Tasaki & Mizutani (1944), Tasaki & Tsukagoshi (1944) and Kuffler & Gerard (1947) have investigated the properties of small motor nerve fibres which supply many frog muscles and observed that these axons produce a slow local potential change in the muscle which is wholly different in character from the usual propagated muscle spike, and which is accompanied by a slower type of contraction. Kuffler, Laporte & Ransmeier (1947) found that the maximum tetanus tension evoked by the small axons was about 10–15% of the normal twitch tension, and they suggest that the small axon system may be used for the maintenance of peripheral 'tonus'. In view of Matthews's (1931 *b*) work, however, there is an alternative possibility, namely that the atypical muscle responses described by Kuffler and his colleagues arose in the intrafusal motor system, and that their function was to regulate the response of the stretch receptor.

To decide between these two propositions, it is necessary to record the activity of nerve and muscle fibres simultaneously and to study the effect on the afferent discharge of the different types of motor axons. If it be true that the small, high-

Anthony Taylor discusses Bernhard Katz's 1949 paper entitled: The efferent regulation of the muscle spindle in the frog. A copy of the paper can be obtained from http://jeb.biologists.org/cgi/reprint/26/2/201.

In this article, we go back over 55 years to the paper by Bernhard Katz in *The Journal of Experimental Biology* (Katz, 1949). Although its subject has since been researched in more detail and with more sophisticated techniques, this paper still has much to teach us regarding clear thinking, simple but elegant experimentation and far-sighted discussion.

By the time of this publication, the classical histological studies of the muscle spindle had shown that it consisted of a bundle of slender striated muscle fibres enclosed in its central region by a connective tissue capsule, in both amphibia and in mammals. The central intrafusal fibres in the muscle spindle are surrounded by sensory receptors that respond to stretch in the muscle. The capsule is surrounded by the extrafusal fibres, which generate the muscle's force. In mammals, there are two types of sensory ending, the large centrally placed primary endings and the smaller adjacent secondary endings (see Ruffini, 1898). Both types connect to the spinal cord *via* myelinated afferent, or sensory, axons; larger and faster for the primaries than for the secondaries. However, only one type of ending, similar to the primary, was seen in amphibia. The intrafusal muscle fibres received a motor nerve supply, which had recently been shown by Leksell to be derived in mammals from a special group of small myelinated axons in the spinal ventral roots and referred to as γ-efferent (Leksell, 1945). Stimulation of these axons caused no detectable contraction but excited an afferent discharge from the spindles. This was seen as a means by which the response of the spindles to muscle length change could be modified by the central nervous system. At the same time it had been found (Tasaki and Mizutani, 1944) that extrafusal muscle fibres in amphibia were innervated by two distinct motor systems. Motor neurons with large axons caused the familiar large fast twitches with single stimuli, known as the twitch system, whilst motor neurons with small axons required repetitive stimulation to cause slow and relatively weak contractions, known as the tonic system.

There were two questions that Katz sought to answer in the frog (Katz, 1949). First, whether the large motor neurons could activate the intrafusal fibres. Second, whether the small muscle fibre system in the frog acted only to generate tonus (a state of prolonged muscle tension) in the extrafusal muscle, as described by Stephen Kuffler and Ralph Gerard (Kuffler and Gerard, 1947), or whether it could also 'regulate the response of the stretch receptor'. Curiously, Katz did not appear to be aware of Leksell's results in the cat (Leksell, 1945) but quoted the suggestion of Matthews that in frogs there was an intrafusal motor innervation from high-threshold axons (i.e. small diameter) distinct from the extrafusal innervation (Matthews, 1931).

As proved to be the case in all of Katz's subsequent work, the preparation was well-chosen and the methods elegantly simple. The small extensor longus digitorum, a lower leg muscle, was isolated with its nerve containing about 12 axons, of which three or four were sensory. One recording electrode was placed on the muscle and another close by on the nerve. Adjacent to this, Katz placed a pair of polarising electrodes to allow for differential and reversible block of conduction in the large motor axons, beyond which were the stimulating electrodes. In essence, he observed that stimulation of large, low-threshold, motor axons not only caused extrafusal contraction but also a short burst of afferent impulses. The afferent firing persisted when extrafusal contraction was blocked by critical dosage with the muscle relaxant curare, thus showing that the large motor axons branched to innervate intrafusal muscle fibres.

Another important finding was that when muscle shortening was allowed, the tendency of extrafusal contraction to silence the spindle was offset by the intrafusal contraction. Katz discussed the significance of this clearly, with the proposal that when an extended muscle is contracted actively in life, the inevitable simultaneous intrafusal contraction would ensure that afferent activity continues, which would support the contraction against loading by means of the stretch reflex. This concept was followed up later by recording the spindle afferent activity from a toad muscle contracting actively against springs of different compliance (Murthy and Taylor, 1970).

One can see in Katz's idea the inspiration for subsequent work in mammals on how the γ-efferent system described by Leksell (Leksell, 1945) could be used in controlling active muscle contraction. It became widely accepted that the γ-efferent neurons are generally activated in parallel with the α-motor neurons that supply the extrafusal muscle, a concept referred to as 'alpha–gamma coactivation'. Despite the apparent success of his method for restricting stimulation to the small motor axons, Katz was not able to show clear evidence for an effect of them on the intrafusal muscle. However, it was later evident that tetanic stimulation is necessary to activate the tonic muscle fibres, which then do indeed excite the spindle afferents (see review by Eyzaguirre, 1962). However, it was not until the work of Brown that the true significance of the fast and slow motor fibres in control of the amphibian spindle became clear (Brown, 1971). The fast group caused an increase in the afferent firing at any given length (biassing) and some reduction in the sensitivity to stretch. The slow group caused a marked increase in stretch sensitivity with little effect on resting frequency. In this way they may be seen to parallel the behaviour of the static and the dynamic γ-motor fibres, respectively, in mammals. These two classes were defined by the effect of their stimulation on the afferent response to controlled muscle stretch (Crowe and Matthews, 1964).

Nothing in science is ever quite new, but in this paper Katz showed ways of studying the complexities of the muscle spindle that have been widely influential since. In 1949, recovery from the chaos of World War II had scarcely started, apparatus was relatively primitive and laboratory facilities improvised. Katz had only returned to England from service in the Royal Australian Air Force in 1946 to join A. V. Hill at University College London. Any lack of resources was more than compensated for by the keen intellectual atmosphere of the time. The frequent meetings of the Physiological Society, rotating around all the Physiology departments, provided unlimited scope for critical discussion of the latest work, and researchers vied with each other to provide vivid live demonstrations (e.g. Katz, 1950). It is evident that Katz was strongly motivated to study the biophysical basis for physiological mechanisms and would choose whatever preparation was most convenient and appropriate for the current task, which at that time was to understand the mechanisms of sensory reception. Consequently, he went on to use the frog muscle spindle to study the local currents leading to the initiation of sensory impulses and made no further contributions to understanding the motor innervation of muscle spindles. Nevertheless, one can see that his one paper on this subject inspired others and started a period of vigorous research, revealing complexities which are still engaging widespread interest amongst students of motor control (for reviews, see Matthews, 1981; Taylor et al., 1999).

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