Editorial Focus

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ESSAYS ON APS CLASSIC PAPERS

The size principle: a rule describing the recruitment of motoneurons

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This essay looks at the historical significance of five APS classic papers that are freely available online:

McPhedran AM, Wuerker RB, and Henneman E. Properties of motor units in a homogeneous red muscle (soleus) of the cat. *J Neurophysiol* 28: 71–84, 1965 (http://jn.physiology.org/cgi/reprint/28/1/71).

Wuerker RB, McPhedran AM, and Henneman E. Properties of motor units in a heterogeneous pale muscle (m. gastrocnemius) of the cat. *J Neurophysiol* 28: 85–99, 1965 (http://jn.physiology.org/cgi/reprint/28/1/85).

Henneman E, Somjen G, and Carpenter DO. Functional significance of cell size in spinal motoneurons. *J Neurophysiol* 28: 560–580, 1965 (http://jn.physiology.org/cgi/reprint/28/3/560).

Henneman E and Olson CB. Relations between structure and function in the design of skeletal muscles. *J Neurophysiol* 28: 581–598, 1965 (http://jn.physiology.org/cgi/reprint/28/3/581).

Henneman E, Somjen G, and Carpenter DO. Excitability and inhibitability of motoneurons of different sizes. *J Neurophysiol* 28: 599–620, 1965 (http://jn.physiology.org/cgi/reprint/28/3/599).

MOTOR AXONS BRANCH in the peripheral nerve to supply muscle fibers in a single muscle; the motoneuron and the dozens to hundreds of muscle fibers it innervates are referred to collectively as the "motor unit." Individual muscles are composed of numerous motor units, ranging from a few to several hundred, depending on the muscle. Contraction of a muscle occurs by activating motoneurons in the pool of motoneurons innervating that muscle. Understanding the control of muscle contraction requires knowledge of how motor units are recruited in response to various inputs. Is the order of recruitment highly variable depending on the task, or is it highly stereotyped?

In 1957, Elwood Henneman (Fig. 1) published a brief report in *Science* (4) demonstrating that single flexor motor axons recorded extracellularly in a ventral root filament were recruited in order of spike height as the intensity of electrical stimulation to the ipsilateral sciatic nerve was increased. Furthermore, the individual axons ceased firing in the inverse order that they were recruited after the stimulus, i.e., first recruited, last derecruited. This finding based on extracellular axon recording, where axon size is proportional to spike height, was generalized to infer that susceptibility to reflex discharge is determined by neuron size, previously shown to be proportional to axon size (3). It was further hypothesized that this rule might apply ubiquitously in the nervous system because the properties of all nerve cells appeared at that time to be, as stated by Henneman (4), "remarkably alike."

In 1965, Henneman and his colleagues published five papers in the *Journal of Neurophysiology* that provided a detailed account of motor unit properties, motoneuron recruitment properties, and how the relationships between these two sets of properties could be summarized in terms of a unifying principle that he called the "size principle." The first two papers, published a few months earlier than the other three, demonstrated motor unit properties for two extensor muscles, the homogeneous soleus (11) and the heterogeneous medial gas-

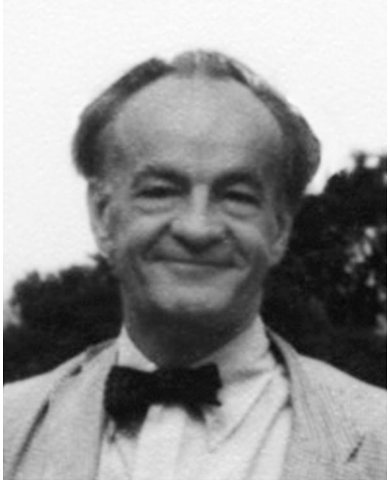

FIG. 1. Elwood Henneman.

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trocnemius (13). A conclusion important for the present discussion was that small axons, in this study based on conduction velocity rather than spike height, supplied motor units generating less tetanic tension than those associated with large axons. In fact, in individual experiments (on cats), the relationship between force and conduction velocity was linear for units whose tetanic tension was less than 20 g. Another important finding was that only units generating the largest forces, found in medial gastrocnemius but not soleus, were subject to fatigue at high rates of stimulation.

The next paper in this series (7) demonstrated that small spikes recorded from ventral roots are recruited before large ones in response to triceps surae muscle stretch in decerebrate cats. The larger spikes were interpreted "as impulses in axons of larger diameter and hence to signify the discharge of larger motoneurons." The first paragraph of the DISCUSSION of this paper contains the first mention of the phrase "size principle" that emerges from the "highly significant correlation between threshold or excitability of individual neurons and the size of the impulses recorded from their axons." It goes on to suggest that "there is a general rule or principle applying specifically to motoneurons . . . according to which the size of the cell determines its threshold. This size principle dictates the order of recruitment in the stretch reflex and . . . the flexor reflex." At the end of this paper, the concept of "usage" is introduced whereby "various cells in a (motoneurons) pool are fired rarely, moderately, or frequently according to their sizes."

The penultimate paper in this series expanded on the concept of motor unit usage (6). Comparison of muscle fibers in medial gastrocnemius and soleus muscles led indirectly to the conclusion that large motoneurons innervate pale muscle fibers that are devoid of mitochondrial ATPase and not in the vicinity of capillary circulation, whereas the red muscle fibers innervated by small motoneurons are rich in mitochondrial ATPase with access to capillaries. The access to oxidative metabolism was considered to be a major factor in making motor units innervated by small motoneurons more resistant to fatigue during tetanic contraction than those innervated by large motoneurons, as would be required for motor units that are more active because of their greater susceptibility to discharge.

The last paper in this important series made the point that synaptic inhibition leads to derecruitment according to axon (motoneuron) size: the last one recruited was the most susceptible to inhibition, presumably because there was less surplus excitation (8). This paper also discussed some important implications of the size principle, notably that it represented a way of maximizing the resolution of motor unit force production, in effect the equivalent of Weber's law, well known for sensory systems. It also discussed constraints in neural organization implied by the size principle, specifically that the input to small and large motoneurons be "equal." This was required because recruitment order was considered to be a property of motoneurons, inasmuch as it was independent of the organization of the synaptic input, i.e., it occurred in response to natural and electrical stimulation where recruitment order of sensory fibers was very different. Because motoneurons of different size had similar voltage thresholds, the crucial property determining systematic differences in recruitment was considered to be their input resistance, such that small motoneurons with less surface area would have higher input resistance and would produce a larger voltage drop for a given synaptic input than large ones. This would allow them to reach threshold at a lower level of synaptic input.

This series of papers struck a very responsive chord in the physiology community: the terms neuroscience and neurobiology had not yet emerged. It linked many concepts (recruitment, usage, synaptic efficacy) and structures (motoneuron, motoneuron pool, muscle, muscle fibers). It was relatively easy to visualize and test in many species, including in humans using electromyogram recordings, and made intuitive sense, at least qualitatively. It led to new experiments, including efforts to test the question of equality of inputs to motoneurons using spike-triggered averaging, a technique developed for this purpose in Henneman's lab (12). In the aggregate, these five papers published in 1965 have been cited about 2,300 times (Science Citation Index).

Burke (2) developed another motor unit classification scheme based on the ability to carry out detailed physiological studies on motoneurons as well as histochemistry on the muscle fibers of the same unit. Motor units were classified into four types based on contraction time, fatigability, and the "sag" property. This led to the conclusion that recruitment order is related to motor unit type (i.e., 4 categories) rather than the finer grain determination of recruitment by motoneuron size; although in many situations the order of recruitment of pairs of motoneurons would be the same in both schemes. Other issues included whether the recruitment order could be altered under some conditions and whether all inputs were equal on small and large motoneurons as originally predicted by Henneman in the last of the 1965 papers (7). Many lively discussions at meetings and in front of posters were centered on these questions. Henneman himself continued to study these problems actively, notably the problem that large motoneurons might be expected to have more boutons per afferent to cover their larger surface area. Such a scheme would cancel out the input resistance differences considered from the very beginning to be responsible for the differences in susceptibility of small and large motoneurons to reach threshold. Henneman championed the idea that inputs to small and large motoneurons, at least from spindle afferent fibers, were organized such that the boutons on large motoneurons were more susceptible to impulse blockade due to more presynaptic branching (9). This would tend to equalize functional inputs (i.e., the number of active boutons) to large and small motoneurons, thus allowing properties of the motoneurons to determine susceptibility to discharge.

Despite disagreement on mechanisms of recruitment, there was agreement that it is orderly, i.e., stereotyped, under most conditions. A very elegant recent study by Zajac and Faden (14) demonstrated that the force exerted by a motor unit was statistically a better predictor of its recruitment order than the conduction velocity of its axon. Nonetheless, this conclusion is similar to that of Henneman, who considered motoneuron size to be a surrogate for motor unit force.

Looking over the entire body of Henneman's work in this area, with publications from 1957 to 1990, it is clear that he always thought computationally about the operation of the motor pool. In 1989, a meeting was held at the University of Arizona in Tucson to "acknowledge the seminal contributions that Professor Elwood Henneman has made to this area of research and to neuroscience in general" (preface to *The Segmental Motor System*; Ref. 1). Henneman wrote a brief introductory chapter entitled "Comments on the Logical Basis of Motor Control" in this book with contributions from many of the speakers at that meeting (5). He began by noting that "outsiders looking at our field are often nonplussed by the absence of theories, rules, laws, and principles that lend meaning and dimension to the experimental findings." He went on to discuss the problem of how one recruits a pool of 300 motoneurons to develop force in a single muscle and suggested that orderly recruitment was in effect a law of combination that dictates the functioning of the motor pool. The computational possibilities are constrained by the anatomy and the physiology of the motoneurons and their inputs. This theoretical approach is an indication of his innovative thinking, inasmuch as computational neuroscience has only recently become an important subdiscipline in neuroscience as experimental results, computational methods, and analytic approaches have become available to investigators to build models of neural function at cellular and network levels. Recruitment of motoneurons remains an important problem in neuroscience that continues to build on the pioneering work on the Size Principle reported by Elwood Henneman and his colleagues in 1965 in the *Journal of Neurophysiology*.

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