

# This Week's Citation Classic™

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**Bárány M. ATPase activity of myosin correlated with speed of muscle shortening.**  
*J. Gen. Physiol.* 50:197-218, 1967.  
[Institute for Muscle Disease, New York, NY]

Pure myosin was isolated from 25 different muscles whose contraction time varied 250-fold. The ATPase activity of the myosins was correlated with the contraction time of their respective muscles, suggesting that the myosin ATPase determines the speed of muscle contraction. [The SCI® indicates that this paper has been cited in over 725 publications. It is one of the five most-cited papers for this journal.]

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"The nature of the muscle engine was one of the primary interests of biochemists in the first half of this century. Engelhardt and Ljubimova discovered that myosin, one of the contractile proteins of muscle, hydrolyzes ATP, the compound which provides the energy for muscular contraction.<sup>1</sup> Subsequently, Engelhardt introduced the term mechanochemistry, i.e., the protein which performs the mechanical work is also an enzyme capable of liberating the energy necessary for the work. This idea was challenged by Straub and Feuer a decade later, who found that the globular to fibrous transformation of actin, the other contractile protein of muscle, is correlated with an ATP to ADP transformation of the nucleotide bound to actin.<sup>2</sup> Straub postulated the term mechano-chemical coupling, i.e., the protein which does the mechanical work carries a prosthetic group capable of changing its chemical energy. In Straub's concept, the energy is built in the structure of the muscle engine. In contrast, in Engelhardt's concept, the energy flows from an outside reservoir to the engine similar to that of a car.

"I, as a student of Straub, had spent many years in his institute in Budapest, Hungary, attempting to prove his theory, and continued this research on my own in America. My

failure, as well as that of others, to find a role for the actin-bound nucleotide in contraction forced me to return to myosin. In collaboration with my wife, Kate Bárány, we isolated pure myosin from the three major types of muscle—skeletal, heart, and smooth—and compared these myosins for their size and shape, digestibility by proteolytic enzymes, sulfhydryl content, and ATPase activity. The only significant difference found was in the ATPase activity. Following the suggestion of the late Ernest Gutmann, we prepared myosin from the slow and fast muscles of various animals and have found much higher ATPase activity in myosin from fast muscle than that from slow muscle. The relationship between speed of muscle contraction and ATPase activity of myosin became clear when myosin from extremely slow muscles, like sloth or turtle, exhibited very low ATPase activity.

"This work was scheduled for presentation at a New York Heart Association symposium. Just before my lecture, fire broke out in the hotel and both the audience and lecturers left the scene. For our results to be known, we had to wait for the publication of the symposium's proceedings. In the meantime, we have shown that cross-innervation of rat muscle, which transforms fast muscle to slow muscle and vice versa, also transforms the ATPase activity of myosin.<sup>3</sup> It was also observed that the ATP-induced conformational change of fast muscle myosin was much larger than that of slow muscle myosin.<sup>3</sup> Finally, by introducing radioactive reagents, capable of forming covalent linkages with myosin, into intact muscle, we have shown that, during contraction, myosin undergoes a conformational change, which is the driving force for generating the tension and the movement.<sup>4</sup> Accordingly, in the muscle engine, the fuel, ATP, changes the structure of the engine, myosin.

"This paper is frequently cited because, in all muscles, the ATPase activity of myosin is related to the speed of contraction. This paper was also the first demonstration of a relationship between the enzymic activity of a pure protein and a basic biological phenomenon, motion."

1. Engelhardt W A & Ljubimova M N. Myosine and adenosinetriphosphatase. *Nature* 144:668-9, 1939. (Cited 220 times since 1955.)
2. Straub F B & Feuer G. Adenosinetriphosphate, the functional group of actin. *Biochim. Biophys. Acta* 4:455-70, 1950. (Cited 185 times since 1955.)
3. Bárány M & Clooe R I. The transformation of myosin in cross-innervated rat muscles. *J. Physiology* 213:455-74, 1971. (Cited 210 times.)
4. Bárány M & Bárány K. A proposal for the mechanism of contraction in intact frog muscle. *Cold Spring Harbor Symp.* 37:157-68, 1972. (Cited 30 times.)