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This Week's Citation Classic

Ebashi S & Endo M. Calcium ion and muscle contraction.
Progr. Biophys. Mol. Biol. **18**:123-83, 1968.
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The contemporary concept (1967) of the roles of Ca ion in muscle contraction is introduced. In the absence of Ca ion, troponin in collaboration with tropomyosin exerts an inhibitory effect on the actin filament, not to interact with myosin. Ca ion discharged from the sarcoplasmic reticulum under the influence of the action potential affects troponin and releases the actin filament from its depressed state, resulting in contraction. The sarcoplasmic reticulum then removes Ca ion from troponin at the expense of ATP and induces relaxation. The importance of Ca ion in other intracellular processes is also discussed. [The *SCI*® indicates that this paper has been cited over 965 times since 1968.]

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"What is described in the summary above is common knowledge and found in ordinary textbooks for college students. However, not so many years have elapsed since the establishment of the Ca concept in muscle contraction. In a symposium on muscle, held in 1962, the above proposal that the Ca uptake of the sarcoplasmic reticulum should be the key mechanism of relaxation was very unpopular; strong ardor for an imaginary 'soluble relaxing factor' was still dominating. A. Weber and I, perhaps the only persons who were convinced of the essential nature of Ca ion in muscle contraction at that time, were having a hard time.

"One of the criticisms offered to me at this meeting was that I should explain the reason why Ca ion was effective only on crude systems such as glycerinated muscle fibers or natural actomyosin (myosin B), but not on pure actomyosin. I was told, 'I cannot accept such a mysterious idea; if Ca ion is the real factor, it must act on the pure system.'

"If I had been allowed to speak in Japanese, I could have somehow refuted this argument. Unfortunately, or fortunately, my poor English could not afford it. As a consequence, I had to answer it by presenting experimental data. This eventually led me to the discovery of the third component[1] other than myosin and actin and eventually of troponin.[2]

"Now Ca ion is no longer the factor unique to muscle contraction, but 'a common mediator between function and metabolism,' as clearly predicted in this article (see p. 160). Perhaps this expression was too modest in view of its universal roles in fundamental biological processes. Now the enthusiasm of biochemists for Ca ion is somewhat similar to that created by cyclic nucleotides some years ago. I am a little worried that such enthusiasm could bring about transcendental belief in Ca ion, as we have often experienced in the history of science.

"This article has two distinct features. One is that it boldly emphasized the importance of Ca ion when most biochemists did not pay any attention to this ion. The other is that regulatory processes were conceptually separated from contractile processes; now the regulatory mechanism is one of the main fields not only in muscle research,[3] but also in biology in general.

"When Endo and I began writing this article at the beginning of 1967, the worldwide students' rebellion had already started in Japan, particularly in our medical school at the University of Tokyo. I was extremely pessimistic about the future of the university and Japanese science. Even such a rational, prudent person with keen insight as Endo did not oppose my desperate opinion. I said inwardly, 'This article could be my last scientific work.' Fortunately we were wrong, but this unusual mental state might have added something to this article."

1. **Ebashi S.** Third component participating in the superprecipitation of 'natural actomyosin.' *Nature* **200**:1010, 1963.
2. **Ebashi S & Kodama A.** A new protein factor promoting aggregation of tropomyosin. *J. Biochemistry* **58**:188-90, 1965.
3. **Ebashi S, Maruyama K & Endo M, eds.** *Muscle contraction, its regulatory mechanisms.* New York: Springer-Verlag, 1981. 549 p.