Meetings

Muscle Contraction

An international meeting on the molecular biology of muscle was held at Endicott House, Dedham, Massachusetts from 23 to 27 May 1962. The following topics were discussed: myosin, actin, interaction of myosin and actin, the structure of striated muscle, the structure of smooth muscle (with particular reference to the "catch" mechanism), energetics of muscle contraction, and theories of muscle contraction. Sixty investigators participated, and the relatively small size of the conference made possible informal and thorough discussion of important problems. The meeting was sponsored by the recently established department of muscle research of the Institute of Biological and Medical Sciences of the Retina Foundation and was supported by a grant from the National Science Foundation.

The conference was opened with remarks by Albert Szent-Györgyi. Two sessions chaired by J. T. Edsall were devoted to the structure and enzymatic activity of myosin. Significant advances were reported in the study of myosin by electron microscopy. R. V. Rice presented electron micrographs of individual myosin molecules; the particles appear as long thin rods terminating in a globular portion, which is probably related to the heavy meromyosin subunit. H. E. Huxley demonstrated in vitro formation of myosin aggregates closely resembling the thick filaments of striated muscle. These tapered fibrils have projections along their length except for a central smooth portion. Huxley suggested that one interpretation of his findings would be that the myosin filament is built initially from an antiparallel dimer. This unit would grow at each end by the addition of molecules polarized so that the rodlike portions point to the central zone (or *M* line); the "bridges" from the heavy meromyosin would project at the surface.

The definitive correlation of these electron microscopic observations and the physicochemical properties of myosin and its subunits remains a central problem. The molecular weight of skeletal and cardiac myosin, the number of polypeptide chains in myosin, and the specific action of proteolytic enzymes on the molecule were not conclusively established. Further insight into these problems was provided by the report of D. Kominz that a helical subunit is obtained from myosin by prolonged treatment with copper cyanide in alkaline solution. Unlike the light meromyosin molecule produced by proteolytic action, this subunit did not depolymerize into "protomyosins" upon treatment with urea.

The mechanism of enzymatic hydrolysis of adenosine triphosphate (ATP) was discussed in the light of recent experiments by Koshland and his colleagues, and of Boyer and Dempsey on the O^{18} exchange between water and inorganic phosphate. There is now agreement among these workers that two exchange processes may occur: one is connected with the hydrolysis of adenosine triphosphate or inosine triphosphate and may be attributed to the existence of a phosphorylated enzyme intermediate; the other exchange occurs with inorganic phosphate present in the medium and is independent of the hydrolytic reaction. Boyer, Dempsey, and Benson also reported that the ratio of O^{18} exchange to phosphate liberated increased in glycerol-extracted fibers when shortening took place under a load; this observation indicates that the mechanism of ATP hydrolysis is influenced by the performance of work.

The two sessions dealing with actin were held under the chairmanship of J. Gergely. An important contribution was the work of J. Hanson and J. Lowy on the electron microscopy of F-actin filaments. The filaments were clearly resolved as a two-stranded helical structure made up of globular units, corresponding to G-actin monomers. There was considerable discussion about the presence of tropomyosin in actin preparations and the possible physiological and structural significance of the interaction between these two proteins. Various other topics were considered: the precise role of ATP hydrolysis in polymerization; the concept of critical concentration introduced by Oosawa and his colleagues; the specificity of bound divalent cations; and the existence of ADP-G actin (Hayashi and Weber).

The session on the structure of striated muscle was held under the chairmanship of H. E. Huxley, who presented electron micrographs showing isolated thin and thick filaments. The attachment of heavy meromyosin to the actin filaments resulted in a structure which revealed a sense of direction in the thin filaments, symmetrical about the *Z* line. F. Pepe described work performed jointly with Huxley on the localization of bound antibody by electron microscopy in intact myofibrils and isolated filaments. Andrew G. Szent-Györgyi spoke on fluorescent antimyosin binding in muscle, suggesting that his observatons could be accounted for by a "migration" of myosin during contraction to the lateral parts of the *A* band. It was agreed that although this evidence should be seriously considered, the problems inherent in antibody techniques require further exploration. R. J. Podolsky presented a film demonstrating that single fibers without sarcolemma (the Natori preparation) failed to contract when stretched to the point of no overlap between the actin and the myosin filaments. This result is in accord with the Huxley-Hanson double-filament model. K. R. Porter showed electron micrographs of filaments within the *Z* line, arranged in a square pattern and connected with the hexagonally arranged actin filaments of the *I* band. (Similar observations have recently been published by Knappeis and Carlsen.)

The structure of smooth muscle, particularly that of "catch" muscles of mollusks, was discussed under the chairmanship of A. G. Szent-Györgyi. Lack of agreement on the nomenclature in this field was again encountered, the terms *tropomyosin A* and *para-*

myosin having been used synonymously for the protein that makes up the major part of the thick filaments of molluscan muscle. J. Hanson presented electron micrographs (obtained with J. Lowy) that demonstrated the presence of only two kinds of filaments in "catch" muscles.

The fact that the paramyosin-containing filaments have free tapered ends, and are therefore discontinuous, was adduced as evidence that paramyosin (tropomyosin A) is not responsible for the "catch" or maintenance of tension. Lowy and Hanson propose that the "catch" in these specialized muscles is due to the slow release of the links formed between actin and myosin in contraction. An alternative point of view was put forward by C. Ruegg, who described experiments in which the actomyosin system was inactivated by various reagents, including thiourea, without concomitant impairment of the "catch" mechanism. W. Johnson and A. G. Szent-Györgyi presented corroborative data indicating a *p*H-dependent phase transition in the paramyosin system of glycerol-extracted fibers. These results supported the view that paramyosin (tropomyosin A) is the component responsible for the "catch" and is distinct from the actomyosin system responsible for the development of tension.

The session on the interaction between myosin and actin, with H. H. Weber as chairman, was dominated by discussion of the relaxing factor in muscle. Although it was generally agreed that the sarcoplasmic reticulum participates in the mechanism of relaxation, the precise mode in which this structural component exerts its effect was not established. In view of the ATP-dependent binding of calcium by the sarcoplasmic reticulum (Ebashi and Hasselbach) and the well-known inhibition of relaxation by calcium, some investigators considered that calcium binding alone may explain the phenomenon of relaxation. Others expressed the view that the elaboration of a soluble relaxing substance by the reticulum could play an important role with or without further calcium binding.

The problems relating to the energetics of muscle were introduced by the session chairman, D. R. Wilkie. R. E. Davies and D. F. Cain reported the disappearance, during the single contraction, of adenosine triphosphate in

frog muscles treated with 1,2,4-fluorodinitrobenzene. This significant observation, if confirmed in other laboratories, should settle the doubts that have persisted for several years about the role of adenosinetriphosphate as the immediate source of energy for contraction.

The last session of the conference dealt with theories of muscle contraction and with some problems related to excitation coupling. The chairman, R. J. Podolsky, ably outlined theories based essentially on the double-filament model. Two alternative schemes were examined: one involved simple sliding of filaments without changes in the structure during contraction; the other was based on the possibility of shortening in the thin filaments. A. G. Szent-Györgyi and W. Johnson proposed a new theory derived from the fluorescent antibody results, in which connections were postulated between the myosin and the actin filaments in opposing halves of the sarcomere. According to their hypothesis, some reorganization or folding within the myosin filaments would pull in the opposing actin filaments during contraction. In the discussion that followed it was noted that no evidence for structural changes in the thick filaments during contraction has as yet been demonstrated.

The participants felt that this had been a useful and stimulating conference, enabling workers in various fields to focus on critical and unresolved problems in the structure and function of muscle.

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Acarology

For the first time in the Western Hemisphere, acarologists from the diverse disciplines of taxonomy, physiology, biochemistry, genetics, disease transmission, behavior, and economic control met together to share their research and to focus upon their mutual concern—acarology. Observers have noted that this historic meeting pushed