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Liquid cell electron microscopy revealed a number of mysteries in molecular mechanism of muscle contraction

Molecular mechanism of muscle contraction has been studied intensively over more than 50 years, since the monumental discovery that muscle contraction results from relative sliding between actin and myosin filaments coupled with ATP hydrolysis. It is generally believed that myosin heads (M) extending from myosin filaments first attach to actin in the form of $M \cdot ADP \cdot P_i$, perform power stroke producing myofilament sliding coupled with release of P_i and ADP, and then detach from actin when next ATP comes to bind it to form $M \cdot ATP$. Myosin heads detached from actin perform recovery stroke coupled with reaction $M \cdot ATP \rightarrow M \cdot ADP \cdot P_i$, and again attach to actin. The amplitude of myosin head power and recovery strokes still remains to be a matter for debate and speculation. As early as late 1980s, we started to visualize ATP-induced myosin head movement in hydrated myosin filaments electron microscopically by using a carbon film-sealed liquid cell. We used synthetic myosin filaments, in which individual myosin heads were position-marked with colloidal gold particles and monoclonal antibodies to myosin head. Filaments were observed under a magnification of 10,000X, and their images were recorded with an imaging plate system. Care was taken to limit total incident electron dose below the value to impair function of muscle proteins. The results obtained are summarized as follows: (1) muscle myofilament sample attach firmly to carbon sealing film; (2) time averaged mean position of individual myosin heads do not change appreciably with time; (3) in the absence of actin filaments, myosin heads move in response to ATP by ~6nm away from the center of myosin filaments, indicating that myosin head recovery stroke takes place without being guided by actin filaments; (4) in the presence of actin filaments, myosin heads perform power stroke in response to ATP with amplitudes depending on experimental conditions.

Biography

Haruo Sugi graduated from Postgraduate School in 1962, in the University of Tokyo with the degree of PhD. He worked in Columbia University as a Research Associate, and in National Institutes of Health as a visiting scientist from 1965 to 1967. He was a Professor and Chairman in the Department of Physiology, Teikyo University Medical School from 1973 to 2004, when he became Emeritus Professor.

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