Structural Dynamics of Actomyosin in Muscle Contraction by X-ray Diffraction/Scattering

Katsuzo Wakabayashi
Osaka University, Osaka, Japan

The sliding or contractile force in muscle is thought to be generated by the interaction of myosin heads projecting from the thick filaments with actin in the thin filaments, powered by hydrolysis of ATP in the sarcomere. X-ray diffraction has provided a structural basis for the mechanism underlying this process, showing that the interaction between actin and myosin heads occurs in incommensuate periodicities of the two filaments. The excellent x-ray diffraction patterns from a contracting muscle have been recorded by using a high-sensitivity, high-resolution storage phosphor area detector. Our analysis showed that during contraction, the structure of the thin actin filaments was altered and that the alteration was accompanied by the elastic extension and twisting of the helical filaments.[1] The amount of the extension of the actin filaments corresponded to 60-70% of the total extention of the elastic elements in the sarcomere which carries active tension.[2] These findings provide evidence that the thin actin filaments are flexible and very pliant, leading us to make a significant modification of the currently accepted "rotating or tilting crossbridge" model. On the other hand, it has been shown by x-ray solution scattering that the global conformational change is isolated myosin heads (subfragment-1, S1) corresponding to an approximate 5-nm movement of the distal end of the molecule occurred during hydrolysis of ATP.[3] The experiments using ATPase intermediate analogs indicated that such a global change occurred in the state of S1*.ADP.Pi, and returned to the original structure in two steps, on release of Pi and release of ADP. This implication has been tested in active muscle by time-resolved x-ray diffraction in a ~0.2-ms resolution using a high-brilliance beam from the undulator installed at the Tristan main ring.[4] On applying a sinusoidal length perturbation at 500 Hz to a contracting muscle, tension changed in phase with the length changes and the intensity of the 14.5-nm myosin-based reflection changed in antiphase with tension changes. The results indicated that there exists a coupling between the force generation and structural changes occurring in the distal portion of myosin heads which are interacting with actin. Several important findings stimulate a sophisticated model in a framework of the coordinated structural changes of actin and myosin heads.

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[1]Wakabayashi and Amemiya, Handbook Synchrotron Rad., 4, 597 (1987); Ueno et al., submitted for publication (1998).
[2]Wakabayashi et al., Biophys. J., 67, 2422 (1994); Takezawa et al., submitted for publication (1998).
[3]Sugimoto et al., Biophys. J., 68, 29 (1995); Sugimoto et al., submitted for publication (1998).
[4]Yagi et al., J. Synchrotron Rad., 3, 305 (1996).