Mechanism of Inter/intra-sarcomere Coordination on Spontaneous Oscillatory Contraction of the Muscle Contractile System

Yuta Shimamoto
Ishiwata Lab, Dept. Physics, School of Science and Engineering, Waseda University
3-4-1, Okubo, Shinjuku-ku, Tokyo, Japan; E-mail: yuta-smt@toki.waseda.jp

The muscle contractile system consists of the regular array of molecular motors (myosin molecules) and a helical track (an actin filament). This system generates stable self-excited oscillation called SPOC (Spontaneous Oscillatory Contraction) in the coexistence of ATP, ADP and Pi without Ca^{2+}. Each contractile unit (i.e. sarcomere) maintains regular waveform composed of slow shortening and quick lengthening. In addition, the lengthening phase propagates to the adjacent sarcomeres along the myofibril. Single molecular motor works stochastically, whereas the biological system, which is organized by thousands of molecular motors, generates well-ordered functions like SPOC. We expect that the self-regulation in the molecular assembly is performed by the inter/intra-sarcomere coordination through the force.

Here, we investigated the mechanical property of sarcomeres in SPOC that is expected to be relevant to the self-regulation mechanism of molecular motors. We applied external load to rabbit psoas myofibrils of which both ends were held auxotonically with a pair of glass micro-needles under the inverted microscope, and observed the response of each sarcomere. Myofibrils under the relaxing condition were activated by adding MgADP (ADP-induced contraction). In both SPOC and the ADP-induced contraction, the myosin-ADP complex is a “regulator” for the activation of thin filaments. Besides, the affinity between myosin and ADP is controlled by the strain, so that the myosin-ADP complex works as a “strain sensor”. Taking the advantage that sarcomeres do not oscillate in the ADP-induced contraction, we could measure the mechanical property of sarcomeres under various loads, loading rates, MgADP concentrations and sarcomere lengths by focusing on the properties of the myosin-ADP complex.

We found that the sarcomeres in the ADP-induced contraction were quickly transformed into a non-force-generating state against quick stretch faster than a threshold rate of stretch. The transition occurred stochastically against the same mechanical perturbations; we found that the probability of the transition depends on the sarcomere length. Besides, the transition probability against stretch was dependent on the MgADP concentration; the higher the MgADP concentration, the smaller the transition probability. In summary, these results indicate that 1) the force can regulate the activation of sarcomeres, 2) the activated state is quasi-stable, being sensitive to the load, 3) the probability of transition from activation to relaxation is controlled by the proportion of the myosin-ADP complex, and 4) the proportion of the myosin-ADP complex changes depending on the phase of SPOC oscillation. It is expected that the mechanical instability of sarcomeres observed here is the basis of the stable periodicity and the phase coordination of sarcomeric oscillations in SPOC.