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Cryo-ET reveals sarcomere structures at molecular resolution

Individual muscle fibers can be very large syncytia of up to several centimeters in length and are comprised of the force-generating and load-bearing devices of muscles called sarcomeres. In my presentation, I will explain how we managed to obtain high-resolution structures of native sarcomeres using cryo-electron tomography (cryo-ET). Our cryo-ET reconstructions reveal molecular details of the three-dimensional organization and interaction of actin and myosin in the A-band, I-band and Z-disc and demonstrate how α -actinin cross-links antiparallel actin filaments. Structures of myosin, tropomyosin, actin, and nebulin at up to 4.5 Å further reveal two conformations of “double-headed” myosin, where the flexible orientation of the lever arm and light chains enable myosin not only to interact with the same actin filament, but also to split between two actin filaments. Our results provide unexpected insights into the fundamental organization of vertebrate skeletal muscle and serve as a strong foundation for future investigations of muscle diseases.

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Host: Patrick Cramer



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