Structural insight into calcium signalling in muscular contraction

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Cryogenic electron microscopy (cryo-EM) allows visualizing biological samples ranging from cells and cellular organelles to individual protein molecules in near-native environment. Method of single particle cryo-EM applies averaging and 3D reconstruction techniques to combine thousands of cryo-EM images of individual proteins or protein complexes and to obtain 3D reconstruction of protein structure at atomic resolution. The application of single particle cryo-EM will be demonstrated on example of structural studies of Ryanodine receptor, an ion channel playing central role in calcium signalling in muscle contraction. Muscle contraction is initiated by the release of Ca^{2+} from the sarcoplasmic reticulum into the cytoplasm of myocytes through ryanodine receptors (RyR). RyRs are the 2.2 MDa homotetrameric ion channels that are primarily gated by changes in concentration of calcium ions in the cytoplasm and are regulated by multiple factors including ions, small organic molecules, and interactions with other proteins. The molecular mechanism underlying the complex regulation of RyR is still poorly understood. I will present the structure of rabbit RyR1 determined by single particle cryo-EM and will show how changes in calcium concentration induce conformational changes in RyR resulting in the channel gating.