

Calcium Storage Protein Calsequestrin

The sarcoplasmic reticulum (SR) plays an essential role in muscle excitation-contraction coupling by regulating the cytosolic free Ca^{2+} concentration. The main SR proteins responsible for this Ca^{2+} regulation is the Ca^{2+} transport ATPase, the Ca^{2+} storage protein calsequestrin (CSQ), and the Ca^{2+} release channel ryanodine receptor.

CSQ, which binds 60-80 Ca^{2+} ions per molecule, represents a ubiquitous, critically important family of Ca^{2+} storage proteins found not only in the SR but also in the endoplasmic reticulum (ER). We have demonstrated a coupling between ion-dependent polymerization of CSQ and its high capacity Ca^{2+} binding.

In order to study the plausible coupling between the Ca^{2+} binding and the polymerization of CSQs, we have for the first time employed Multi-Angle Light Scattering (MALS) for the *exact* measurement of Ca^{2+} dependent polymeric state of CSQs. We have monitored the elution profiles of CSQs in size exclusion chromatography at various Ca^{2+} concentrations using a DAWN EOS (operating at $\lambda=690$ nm) light scattering and an Optilab differential refractometer, the combination of which allows the determination of the absolute molecular weight across the chromatographic peaks.

We found that at a fixed K^+ concentration of 300mM, increasing Ca^{2+} concentration results in transitions from monomer to dimer and to tetramer. If the Ca^{2+} concentration is fixed, *increasing* K^+ concentration results in a shift toward monomers, and *decreasing* K^+ concentration generates polymers.

These data are the *first* demonstrating the interplay of monovalent and divalent cations on the polymeric behavior of purified CSQ, strongly suggesting that CSQ polymerization is under dynamic regulation by mono- and divalent cations. Coincidentally, Ca^{2+} movement in and out of the SR is always accompanied by the opposing flux of monovalent cations.



Crystal structure of tetrameric calsequestrin

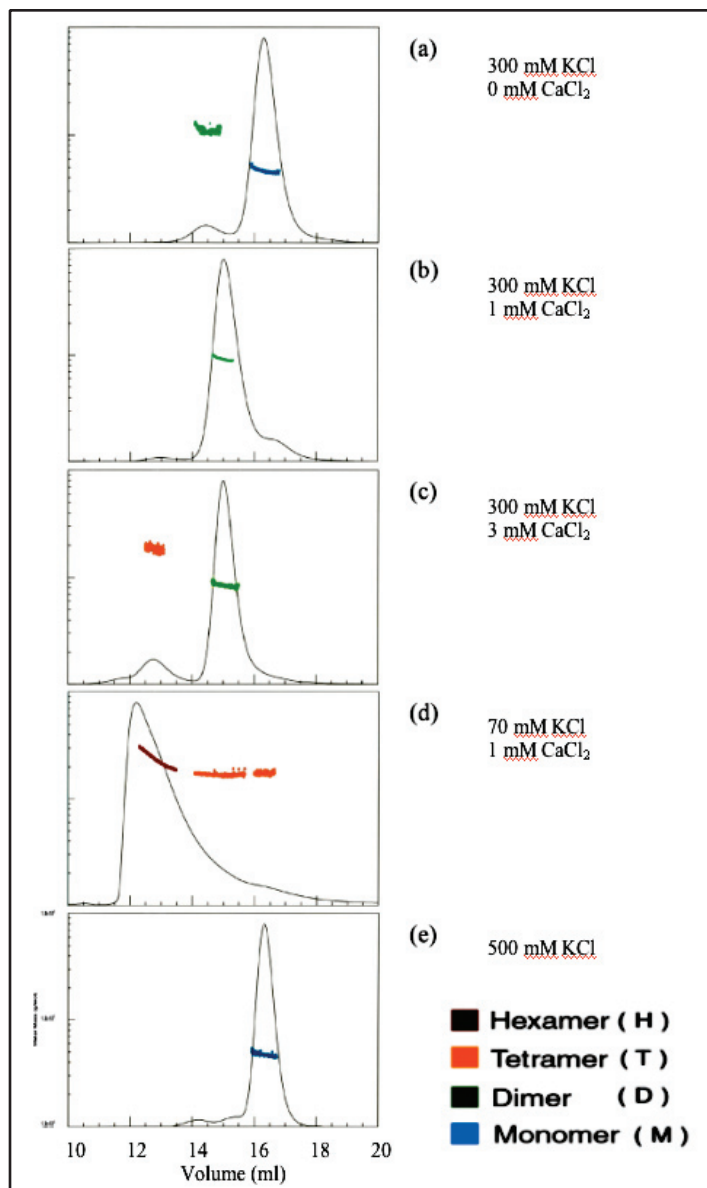
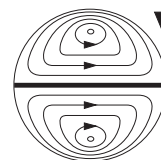


Figure 1. Polymer states of skeletal calsequestrin in different ionic environments; the molecular weights are depicted with different colors.

This note graciously submitted by Dr. ChulHee Kang, Edward Meier Distinguished Professor of Biochemistry & Biophysics, Director of BXRC Center School of Molecular Biosciences, Washington State University, Pullman, WA



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