O-15.4 Short talk

On the Self-Assembly of the Molecular Chaperone αB-Crystallin

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The molecular chaperone αB-crystallin contributes to healthy proteostasis by limiting the amyloid formation of several proteins linked to neurodegenerative diseases, such as α-synuclein, amyloid β peptides, β2-macroglobulin, and more. The active subunit of αB-crystallin has been suggested to be the dimer; however, αB-crystallin has consistently been found in multimeric constellations. Despite the vast number of studies on αB-crystallin, there is no consensus regarding its size distribution at equilibrium. Collectively, studies report a size distribution ranging from 10 – 40 monomers, where some studies argue a narrow distribution and some report a broad distribution. Through size-exclusion chromatography, negative stain electron microscopy, dynamic and static light scattering, small-angle X-ray scattering, and microfluidic diffusional sizing over a broad concentration range, our work shows that αB-crystallin self-assembly assumes a monodisperse-like behavior. Our results indicate that recombinant αB-crystallin forms stable quasi-spherical aggregates of approximately 18-20 monomers independent of the protein concentration. A highly optimal aggregation number that is concentration independent suggests that the self-assembly of αB-crystallin is well described by the closed association model.