

Abstract Submitted
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Computational modeling of protein folding assistance by the eukaryotic chaperonin CCT¹ MANORI JAYASINGHE, GEORGE STAN, University of Cincinnati — Chaperonins are biological nanomachines that promote protein folding using energy derived from ATP hydrolysis. They are found in all the three domains of life and are grouped into two distinct classes based on their lineage. Group I chaperonins represented by GroEL of *E. coli*. bind substrate proteins through hydrophobic interactions. By contrast, group II chaperonins are suggested to use both hydrophobic and hydrophilic interactions to recruit substrate proteins. We focus on the substrate binding mechanisms of eukaryotic (Group II) chaperonin CCT. To this end, we study the interaction of CCT with Tubulin, one of the major substrates. Using molecular docking and molecular dynamics simulations, we probe binding of the β tubulin peptide (205-274) to the CCT γ apical domain. We identify two binding mechanisms, one involving mostly hydrophobic interactions with a helical region, which is structurally equivalent to the binding site of the bacterial chaperonin and a second one involving hydrophilic interactions with a helical protrusion region. Our results suggest that the substrate binding in CCT is highly specific, involving both electrostatic and hydrophobic interactions. These mechanisms likely to be optimized for specific substrate protein-CCT subunit pairs.

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