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Coarse-grained model of chaperonin-mediated protein folding
GEORGE STAN, National Institutes of Health, D. THIRUMALAI, GEORGE LORIMER, University of Maryland, BERNARD BROOKS, National Institutes of Health — Chaperonins are biological nanomachines that employ a spectacular mechanism for simulated annealing. During the chaperonin cycle, concerted, large scale, rigid body conformational changes, ultimately driven by ATP hydrolysis, result in a dramatically expanded chaperonin cavity serving as folding chamber. Chaperonins repeatedly bind misfolded proteins, randomly disrupt their structure, and release them in less folded states, allowing these substrate proteins multiple opportunities to find pathways leading to the native state. What is the fate of the non-native protein during the chaperonin cycle? We addressed this question using coarse-grained molecular dynamics simulations. We find that the fundamental annealing function of the GroEL chaperonin consists of forced unfolding and refolding of the substrate protein. The annealing action is related to the change in the nature of the interaction between the substrate protein and the GroEL particle from predominantly hydrophobic to largely hydrophilic. To identify the proteins most likely to be natural substrates for GroEL we use a bioinformatic approach. Our hypothesis is that natural substrates contain patterns of residues similar to the co-chaperonin GroES.

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