

Abstract Submitted
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Structure, function and folding of phosphoglycerate kinase are strongly perturbed by macromolecular crowding.¹ ANTONIOS SAMIOTAKIS, University of Houston, APRATIM DHAR, SIMON EBBINGHAUS, LEA NIENHAUS, University of Illinois, DIRAR HOMOUZ, University of Houston, MARTIN GRUEBELE, University of Illinois, MARGARET CHEUNG, University of Houston — We combine experiment and computer simulation to show how macromolecular crowding dramatically affects the structure, function and folding landscape of phosphoglycerate kinase (PGK). Fluorescence labeling shows that compact states of yeast PGK are populated as the amount of crowding agents (Ficoll 70) increases. Coarse-grained molecular simulations reveal three compact ensembles: C (crystal structure), CC (collapsed crystal) and Sph (spherical compact). With an adjustment for viscosity, crowded wild type PGK and fluorescent PGK are about 15 times or more active in 200 mg/ml Ficoll than in aqueous solution. Our results suggest a new solution to the classic problem of how the ADP and diphosphoglycerate binding sites of PGK come together to make ATP: rather than undergoing a hinge motion, the ADP and substrate sites are already located in proximity under crowded conditions that mimic the in vivo conditions under which the enzyme actually operates.

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