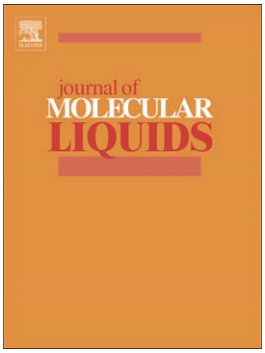

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PII: S0167-7322(16)32953-1
DOI: doi:10.1016/j.molliq.2017.03.030
Reference: MOLLIQ 7065

To appear in: *Journal of Molecular Liquids*

Please cite this article as: Gargi Borgohain, Sandip Paul, Folding/Unfolding of Protein Trp cage in Aqueous Osmolyte Solutions Under Polar Confinement, *Journal of Molecular Liquids* (2017), doi:10.1016/j.molliq.2017.03.030

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Journal of Molecular Liquids 00 (2017) 1–19

Journal of Molecular Liquids

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Folding/Unfolding of Protein Trp cage in Aqueous Osmolyte Solutions Under Polar Confinement

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Abstract

Folding/unfolding processes of the protein Trp cage in presence of osmolytes inside a polar confinement is investigated using replica exchange molecular dynamics (REMD) simulation. A near spherical fullerene like ball consisting of 2940 carbon atoms (charged atoms) is used as a polar confinement. Urea exerts its action profoundly on the protein causing denaturation. Counteraction of TMAO is also observed in ternary solution of urea and TMAO. It is found that TMAO exerts its action in ternary mixed urea-TMAO solution by (i) removing some of the urea-TMAO hydrogen bonds, (ii) preserving the angles and distances between the aromatic planes of the residues Pro17, Pro18 and Pro19 with the indole ring of Trp6 and (iii) retaining the hydrophobic core of the protein Trp cage.

Keywords: Trp cage, REMD, polar confinement, urea, TMAO.

1. Introduction

Protein folding and unfolding are the fundamental processes that occur in cellular environments and are difficult to characterize in detail. 20% – 40% of the cytoplasmic volume is occupied by cellular macromolecules[1, 2, 3, 4, 5]. The crowded cytoplasmic environments significantly influence the biological processes including protein folding/unfolding equilibrium. The effect of crowding environment or the effects arising due to a chaperonin cavity on the protein can be mimicked by considering the protein within a spherical cavity[1, 2]. Chaperones are known as essential units that assist folding of newly synthesized proteins in vivo[6, 7]. GroEL/GroES is the most common example of chaperonin system that facilitates folding of a wide range of bacterial and eukaryotic proteins[6, 7, 8]. A key aspect of the chaperonin is the hydrophobic regions of the cavity that acts as the binding sites for exposed hydrophobic regions of non native protein and the cavity becomes hydrophilic upon ATP/GroES binding[9, 10, 11]. Combined effects of hydrophobic and hydrophilic regions of GroEL/GroES accomplish folding of protein. Brinker et al.[12] showed that GroEL/GroES chaperonin smoothen up the energy landscape of the protein and prevents kinetically trapped intermediates. In literature, numerous experimental techniques and theoretical methods have been reported addressing the effects of confinement on protein stabilization [13, 14, 15, 16, 17]. Tian et al.[13] addressed the effects of polar and non polar confinement on protein folding/unfolding equilibrium.

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