Flexibility of Hunam Thioredoxin 1 and new biding sites using Normal Modes Analysis

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The thioredoxin (Trx) is a ubiquitous protein, present since bacteria to humans. The Thioredoxin system (thioredoxin, thioredoxin reductase and NADPH) is involved in several processes such as oxidative stress, DNA repair, apoptosis, transcription In this work, we used normal mode analysis to identify putative biding site regions for HumanThioredoxin 1 that arise from global motions of its structure. We identified three possible binding regions for inhibitors that corroborate experimental indications. We show that the motions of the protein can expose hydrophobic regions and non-active site cysteines that could constitute biding sites for new inhibitors of the Thioreoxin system. It may be concluded that NMA is an appropriate technique for the characterization of global motions allowing to identify putative binding sites in a proteins.

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