

Higher Internal Flexibility Increases Protein Stability: Solution Structure and Hydrogen Exchange Behavior of *Mj*TRX

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Various factors contribute to protein stability but it is not yet clear how hyperthermophile protein can survive at above water-boiling temperature. We determined the solution structure and thermodynamic parameters of a thioredoxin from the hyperthermophilic archaeon *Methanococcus jannaschii* (*Mj*TRX) and compared to protein flexibility to investigate the contribution of entropy to protein stability. The solution structure of *Mj*TRX retains so-called 'thioredoxin fold' but lacks the N-terminal β -sheet and α -helix compared to *E. coli* thioredoxin, which is similar to a glutaredoxin. *Mj*TRX has lower unfolding entropy indicating that it is more flexible in the folded state compared to *E. coli* thioredoxin. The internal flexibility measured by hydrogen-deuterium exchange rates of amide protons indicates that *Mj*TRX is more flexible than expected from its thermodynamic stability. This showed that increased internal flexibility of protein could increase the protein stability in contrast to the belief that the compactness of protein is a main contributing factor to protein stability.