1078-92-406 **Joanna I Sulkowska*** (jsulkow@physics.ucsd.edu), 9500 Gilman Drive, La Jolla, CA 93037, **Jeff K Noel**, 9500 Gilman Drive, La Jolla, CA 92037, and **Jose N Onuchic**, 9500 Gilman Drive, La Jolla. *Folding mechanism of the smallest knotted protein.*

The tangling of biophysical objects such as proteins is mysterious. For example, it was long believed that proteins would not create knots since this complicates folding. Recent experiments confirmed their existence, however folding from a fully extended polypeptide has not yet been observed. Understanding the mechanism of folding knots is a current challenge for both experimental and theoretical investigation. Recently using molecular dynamics simulations with structure-based, protein models (SBM) we found that three proteins with different folds but the same topology of trefoil knot show the same folding mechanism. These studies suggest that folding the knot involves the protein terminal threading across a native-like loop, formed in a pre-ordered intermediate. During threading the terminal takes from of so called plug or slipknot motif. SBM neglect residual energetic roughness that may become important in exotic protein conformations such as threading polypeptide loops. To understand energetic advantage of slipknot motif during folding we performed detailed atomic simulations of these threading events, starting from conformations obtained from SBM. Completed threading events, both plugging and slipknotting, starting from pre-ordered intermediates were observed. (Received December 13, 2011)