



Protein Folding on the Ribosome: Pulling on Single Nascent Chains with Optical Tweezers

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Abstract:

Proteins are synthesized by the ribosome and generally must fold to become functionally active. Although it is commonly assumed that the ribosome affects the folding process, this idea has been extremely difficult to demonstrate. We have developed a novel experimental system to investigate the folding of single ribosome-bound stalled nascent polypeptides with optical tweezers. This approach has allowed us to follow the folding of single nascent polypeptides of defined lengths in their native environment of the ribosome. We find that the ribosome profoundly decelerates folding of T4 lysozyme, the model protein in our studies. This kinetic mechanism may ultimately promote efficient folding, as it contributes to preventing premature misfolding that we observe with incomplete T4 lysozyme polypeptides in the absence of the ribosome. Our experimental approach opens new avenues for mechanistic studies of *de novo* protein folding and will help to elucidate the contributions of nascent chain-binding molecular chaperones.

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