Protein Folding in vivo is a non-equilibrium process

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Protein re-folding experiments have led to the thermodynamics hypothesis according to which the native structures of proteins are uniquely defined by their primary sequences. However, a growing body of experiments has revealed the important role ribosomes have in co-translational folding, and there is even direct evidence that folding in vivo is a non-equilibrium, kinetic, process (published in: Alexander L et al. (2019) Nat Commun 10, 2709). In a dynamical process it is possible to ensure that the structural outcome is always the same, first, if the starting structure is always the same and, second, if the pathway followed from the initial structure is always the same as well. A non-equilibrium, dynamical pathway for protein folding in vivo that follows those two rules has been previously proposed in: Cruzeiro L (2020) Pure Appl. Chem. 92, 179-191. The idea is that the nascent chain of proteins is helical and that the first step in the folding pathway is the bending of that helix at specific amino acid sites. In this presentation, statistical evidence (previously published in: Cruzeiro L (2021) Biomolecules 11, 357), and dynamical simulation evidence will be presented in support of the proposed pathway.