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INVITED SPEAKER: Replica Exchange Wang-Landau Simulation of Lattice Protein Folding Funnels

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Abstract content
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Understanding protein folding remains a Grand Challenge problem of modern science. The resolution of Levinthal's paradox concerning the ability of proteins to fold rapidly postulates the existence of a rough, "folding funnel" in free energy space that "guides" the protein to its lowest free energy, native state. The funnel is always portrayed schematically as a function of some unknown reaction coordinate and has never actually been observed. We have studied the folding of the protein ribonuclease A by mapping it onto a 124 monomer, coarse-grained lattice HP model [1] and an H0P model [2] that includes "neutral" 0-mers in addition to the hydrophobic H-mers and polar P-mers. (Amino acids are mapped onto one of the three different kinds of monomers, according to hydrophobicity.) Using Replica Exchange Wang-Landau sampling [3], we determined the density of states g(E) to high precision. From g(E) we then calculated the free energy of the protein vs end-to-end distance as a function of temperature. The HP model shows a rather shallow and flat free energy minimum, reflecting the high degeneracy of the ground state. In contrast, the H0P model develops a clear, rough free energy funnel with a relatively low degeneracy ground state. Unlike the common, schematic figures, we find an asymmetric folding funnel that also changes shape substantially as the temperature decreases. Even the location of the free energy minimum shifts as the temperature decreases. To our knowledge, this is the first actual observation of a folding funnel, and its dynamic nature alters our perception of this fundamental concept.

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[2] G. Shi, A. C. K. Farris, T. Wuest and D. P.Landau. J. Phys: Conf. Ser. 686, 012001 (2016)
[3] T. Vogel, Y. W. Li, T. Wuest and D. P. Landau, Phys. Rev. Lett. 110, 210603 (2013)

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