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Abstract for an Invited Paper
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Max Delbruck Prize in Biological Physics Lecture: Single-molecule protein folding and transition paths[1]

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The transition path is the tiny fraction of an equilibrium molecular trajectory when a transition occurs by crossing the free energy barrier between two states. It is a uniquely single-molecule property, and has not yet been observed experimentally for any system in the condensed phase. The importance of the transition path in protein folding is that it contains all of the mechanistic information on how a protein folds. As a major step toward observing transition paths, we have determined the average transition-path time for a fast and a slow-folding protein from a photon-by-photon analysis of fluorescence trajectories in single-molecule FRET experiments. While the folding rate coefficients differ by 10,000-fold, surprisingly, the transition-path times differ by less than 5-fold, showing that a successful barrier crossing event takes almost the same time for a fast- and a slow-folding protein, i.e. almost the same time to fold when it actually happens.

[1]This work was carried out in collaboration with Hoi Sung Chung.