MAR12-2011-003612

Abstract for an Invited Paper
for the MAR12 Meeting of
the American Physical Society

The impact of conformational transformations on the pathways and kinetics of protein self-assembly into extended matrices[1]

JIM DE YOREO, Lawrence Berkeley Nat'l Lab

The concept of a folding funnel with kinetic traps is used to describe folding of individual proteins. Using in situ AFM to investigate both collagen fibril and S-layer membrane assembly on mica, we show this concept is equally valid during self-assembly of proteins into extended matrices. Moreover, considering the conformational changes required to achieve the ordered structure is critical to understanding the pathway to the final state and the kinetics of assembly. In the collagen system, both the pathway and the final conformational state can be finely tuned by varying the ionic strength. This alters the relative strengths of the collagen-collagen and collagen-mica binding free energy, which we quantify using dynamic force spectroscopy. Moreover, when conditions result in the ordered D-band structure of collagen, the emergence of order catalyzes the further transformation leading to non-linear attachment kinetics. In the S-layer system, there is a kinetic trap associated with conformational differences between a long-lived transient state and the final stable state. Both ordered tetrameric states emerge from clusters of an amorphous precursor phase, however, they then track along two different pathways. One leads directly to the final low-energy state and the other to the kinetic trap. Over time, the trapped state transforms into the stable state. By analyzing the time and temperature dependencies of formation and transformation we find the energy barriers to formation of either state to be nearly identical, but once the high-energy state forms, the barrier to transformation to the low-energy state is large. Thus the transient state exhibits the characteristics of a kinetic trap in a folding funnel.

[1]This work was performed at the Molecular Foundry, Lawrence Berkeley National Laboratory, with support from the Office of Science, Office of Basic Energy Sciences, of the U.S. DoE under Contracts No. DE-AC52-07NA27344 and DE-AC02-05CH11231.