Thermodynamics of dna nanostructures and of their folding intermediates

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DNA single strands can be programmed to self-assembled in well determined nanostructures. The program essentially consists of a set of small single strands that hybridizes specifically with a long single stranded scaffold of several thousands bases. The final shape is designed according to geometric constraints imposed by the DNA double helix. The program insures that the complementary pairing is maximized and thus minimises the free energy. Although the design of complex shapes has been successful, little work yet has devoted to the understanding of the folding process.

By analogy with the folding problem of proteins, our current picture of the understanding of the process is to consider a free energy landscape steering the folding of the chemical species into the thermodynamic minima through valleys and passes as well as kinetic traps. Nanostructures are optimized with respect to their thermodynamic properties but not yet with respect to their folding pathway. Such optimization may be relevant to target applications in medicine or cell biology where the folding will take place in a complex environment.

We propose to use differential scanning calorimetry to probe folding intermediates of DNA nanostructures. Our finding indicates that in the case of small model nanostructures it is possible to deconvolute the folding and unfolding of the structure with a reduced set of intermediate states with different thermodynamic properties. In the case of larger origami structures the deconvolution is not possible. Instead we model the folding and unfolding with a reduced set of independent but thermodynamically identical binding reactions. This led us to the concept of super-cooperativity.

We will also discuss the extension of other thermodynamic methods to study the folding process of DNA nanostructures.