Progress in Designing Nucleic Acid Structures and Fine-tuning Their Interactions

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The prediction of the structure of biological macromolecules at the atomic level and the design of new meta-stable structures and secondary interactions are critical tests of our understanding of the structures and the inter-atomic forces that underlie molecular biology. The capacity to accurately predict and design new structures and interactions will allow us to create nucleic acid sequences that will fold in new and useful ways. Here we present some results to demonstrate the progress we have made in designing and assembling new nucleic acid structures that will make an increasingly important contribution to biology and medicine. We call the reaction cycle that exemplifies our approach 'A handshake from a hairpin on the way to a double helix.' In this paper we describe a new 'strand displacement strategy' (SDS). The goal of the project will be to demonstrate that DNA sequences can fold into a variety of meta-stable states that can reversibly unfold into a random coil and refold into the initial state. Small variations of the sequence (mutations), pH, or ionic strength (environment) can shift the equilibrium between neighbouring states drastically in the direction of a different meta-stable state. These shifts between conformers can i.a. be the course for a series of debilitating diseases (triplet repeat diseases).