Thermodynamic analysis of the folding pathway of DNA self-assembled nanostructures

C. Coilhac[1,2], S. Torrengo[3], O. Bourgeois[1], D. Gasparutto[3] and H. Guillou[1,2]

1 Institut Néel, CNRS et Université de Grenoble Alpes (UGA)
2 UGA
3 SPrAM-CEA-Grenoble, CNRS-UGA

The self-assembly property of DNA makes possible the creation a large variety of nanostructure from DNA. The most famous is the DNA origami in which a genome of a virus is folded on himself with a great number of short DNA strands called staples. The folding or unfolding of DNA nanostructures is highly cooperative: the most stable staples that fold first, help the less stable to hybridize with the scaffold [1]. Recently it has been shown that it is possible to steer the folding pathway by design [2] or by a tight control and titration of the staple mixtures [3]. Yet the design of DNA origami is solely based on geometric constraints. A better evaluation of the folding pathway and folding intermediates is relevant to apply and develop DNA origami science to the field of medicine and molecular robotic where complex and computational structures are targeted.

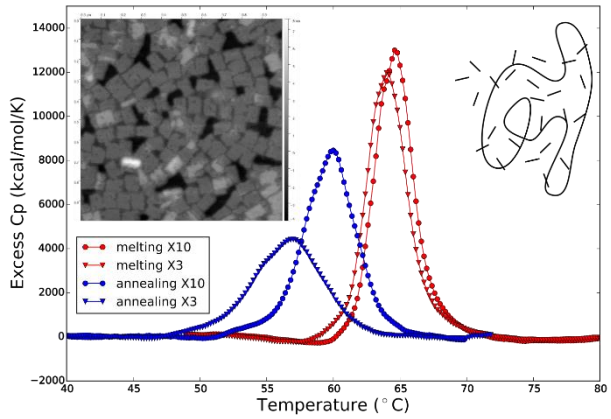

Figure 1: Flat rectangle DNA Origami folding and unfolding transitions measured with DSC. Left inset shows AFM image of the formed origami (scan range 1µm), right inset indicates the unfolded state with the M13mp18 scaffold and the mixture of staples.

We propose to evaluate the folding pathways and the yield of folding by using differential scanning calorimetry (DSC). We selected two model structures that are the DNA tetrahedron described in [4] and a 2D DNA origami. The tetrahedron is made of four strands of equal size spanning each face of the structure while the origami is a much larger structure. The DSC measurements enable us to have information on the number of transitions state and the yield of folding. The figure 2 shows excess heat capacity measured for the origami with two different excess of staples.

1. Arbona, J. M., Aimé, J. P., Elezgaray, J., *Cooperativity in the annealing of DNA origamis,* The Journal of chemical physics *138*(1), 015105, 2013
2. Dunn, K. E., Dannenberg, F., Ouldridge, T. E., Kwiatkowska, M., Turberfield, A. J., Bath, J., *Guiding the folding pathway of DNA origami*, Nature 525, 82, 2015
3. Lee Tin Wah, J., David, C., Rudiuk, S., Baigl, D., Estevez-Torres, A., *Observing and Controlling the Folding Pathway of DNA Origami at the Nanoscale*, *ACS nano 10, 1978-1987*, 2016
4. Goodman, R. P., Berry, R. M., Turberfield, A. J., *The single-step synthesis of a DNA tetrahedron*, Chemical Communications 12, 1372-1373, 2004