Nanofabrication by self-assembly: pathways and defects

Jacob Majikes,[1] Michael Zwolak,[1] J. Alexander Liddle[1]
[1]*Physical Measurement Laboratory, National Institute of Standards and Technology, 100 Bureau Drive, Gaithersburg, MD 20899*
liddle@nist.gov

Self-assembling systems hold great promise for the large-scale, low-cost production of functional nanostructures. The suitable applications of self-assembly methods are ultimately determined by the combination of achievable defect levels and the availability of strategies to mitigate the impact of those defects on overall device/system performance.

The number and nature of the defects formed are controlled by the interplay of kinetics, thermodynamics, and assembly pathway. In IC fabrication, processes operate at high energy scales relative to those of the materials involved, resulting in a minimal equilibrium defect population. Defects may be engineered out, if the correct fabrication sequence (path) is followed.[1] In contrast, self-assembling systems are typically processed so as to approach the equilibrium state. Under these conditions, it is critical to understand the level of control provided by a quasi-static assembly process - defined by thermodynamic equilibrium at each step - and the role of kinetics. The latter often decrease yield *via* trapping in undesirable states. However, engineering the (folding) pathway can increase yield by leading the structure into a metastable - but long-lived - desirable state.

DNA origami is an ideal system in which to explore some of these effects. Here, we use a simplified structure with only a single fold to investigate the contributions of entropy and enthalpy to structural stability as measured by melt temperature (**Fig. 1**). We then vary the excess concentration of the fold oligomer to control yield by changing assembly conditions, and uncover the counterintuitive result that the cooperative effect of the ≈ 200 folds in origami dramatically improve yield and stability (**Fig. 2**). Finally, we will present data on the effect of molecular crowding. These results suggest strategies for improving yield. However, neither alone, nor in combination, will they improve yield to levels common in IC production. To realize the goal of atomically-precise manufacturing,[2] we must develop analogs to the error detection/correction techniques used by biological systems. We speculate that the only effective and scalable approach is to construct, *via* self-assembly, artificial molecular recognition systems[3] to purify perfect products. In addition, to overcome the kinetic limitations of diffusion-driven self-assembly, powered, dissipative devices must also be developed. These directions will not only improve bottom-up/hybrid fabrication techniques – enabling the construction of novel devices in the process – but also shed light on how biology performs its magic.

[1] Moore, Gordon E., Electronics **38**, 114 (1965).
[2] J.N. Randall, et al., Micro and Nano Engineering **1**, 1 (2018).
[3] X. Ouyang, et al, Angewandte Chemie **129**, 14615 (2017).

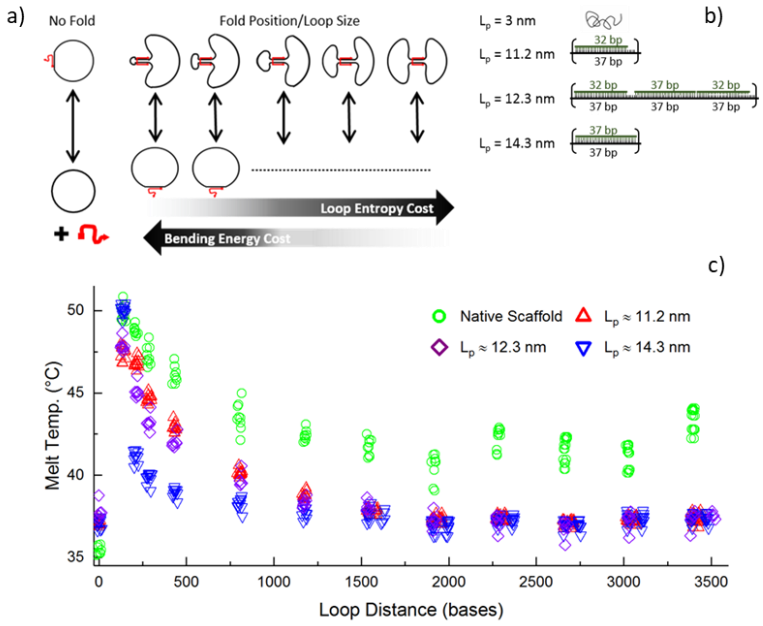

Figure 1. a) Schematic of single fold model DNA origami structure showing how varying fold (loop) distance changes the balance between enthalpic and entropic energy. b) Changing relative fraction of single and double stranded DNA varies persistence length. c) Melting temperature as a function of folding distance for different persistence lengths. Longer fold distances result in larger entropic penalties, reducing melt temperature. Longer persistence lengths incur larger bending energy penalties over all folding distances. Shorter fold distances have higher local concentrations, increasing melt temperatures.

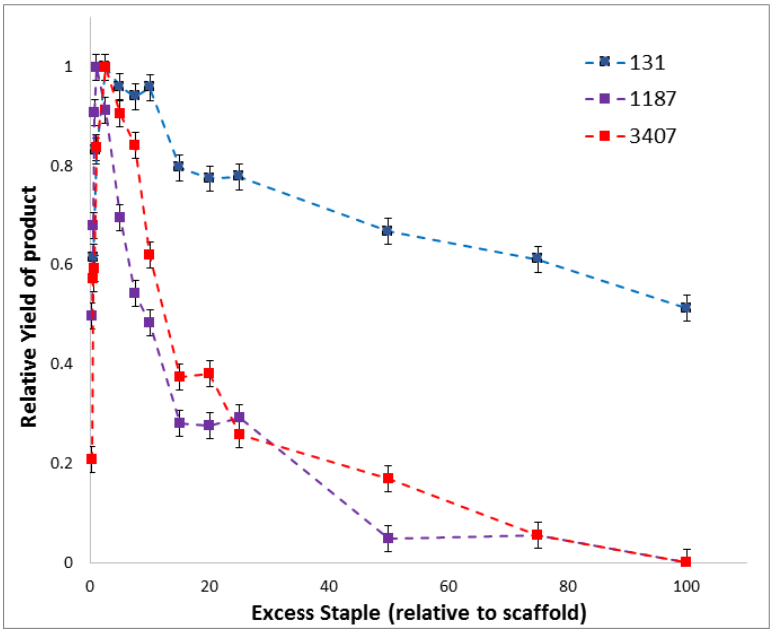

Figure 2. Relative yield as function of folding strand excess concentration relative to scaffold strand concentration. Yield increases linearly up to 1:1 stoichiometry, then decreases approximately as 1/excess. This behavior results from the ability of folding strands to bind at one or both complementary locations on scaffold strand. At high concentrations, both binding sites are occupied by two different folding strands, preventing folding by a single strand from occurring.