Stabilization of DNA Origami Nanostructures by Chemical Ligation

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DNA nanotechnology[1] has been exponentially growing over the last few decades, and with the introduction of scaffolded DNA origami method[2] it has gained much attention. The versatility in designing complex nano-architectures and fully addressable nature have made them the novel scaffolds in various biochemical applications.[3] Regardless of the advantages offered, these nanostructures have very low stability to undergo any further modifications required for various applications. This is due to the presence of many discontinuities (nicks) in the phosphate backbone of the staple strands in the DNA origami nanostructures. Though enzymatic ligation is commonly used in molecular biology to seal the nicks in the duplex DNA, their use is limited and less characterized.

In our previous work[4] we were able to successfully optimize the conditions and characterize the enzymatic ligation of 2D DNA origami. Although the results are promising with a maximum ligation efficiency of ~55%, the complete ligation of all the nick sites is still challenging and limited by the high steric hindrance of the tightly packed DNA origami nanostructure. The alternate method is the chemical ligation of DNA origami which offers advantages over enzymatic ligation by complete accessibility and fast reaction kinetics. However, chemical methods that introduce cross-links when ligated are not suitable to achieve native ligation of DNA origami nanostructures. In this work, we demonstrate the chemical ligation[5] for DNA origami which offers both the superior accessibility to the nick sites and native ligation along with completed reaction much faster than the enzymatic ligation. A detailed analysis and characterization of the chemical ligation will be discussed.

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