Cosolvent Improves the Enzymatic Ligation of DNA Origami

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The invention of structural DNA nanotechnology has led to the creation of various two- (2D) and three-dimensional (3D) structures in the size range of ~10-20 nm. During the past one and a half decades, the field has seen enormous growth due to the addition of the scaffolded DNA origami method[1] which enabled the synthesis of nanostructures with ~100 nm in diameter. Since then various structures have been synthesized with sub-nanometer addressability, and also self-assembled to create even larger structures in micrometer scale.[2] These structures have been used for the nanopatterning of various nanoparticles and quantum dots, attachment of carbon nanotubes, immobilization of biomolecules, carriers of drugs, and for the analysis of single molecular reactions and processes.[3-4]

Despite the proof-of-concept demonstrations on the applications, the real-life utilization of the origami materials is limited due to their insufficient stability. There have been limited efforts to stabilize the DNA origami against thermal, mechanical, and chemical modifications. These limited strategies relied either on the enzymatic ligation of staple strand nicks or by photo-chemically cross-linking the two strands of duplex DNA in the origami. We have recently performed a detailed characterization on the enzymatic ligation of 2D DNA origami to establish the optimized conditions.[5] Under the optimized conditions, up to 10 staples ligation with a maximum ligation efficiency of 55% was achieved. Also, the ligation is found to increase the thermal stability of the origami as low as 5°C to as high as 20°C, depending on the structure. Besides our initial demonstration, due to the tightly packed anti-parallelly oriented arrangement of multiple duplexes in the origami and the difficulties in the accessibility of the nicks by ligase, enzymatic ligation was only partly successful. To further enhance the enzymatic ligation of origami, we have carried out the effect of cosolvent, and identified the best performing cosolvent. Our results indicated that the cosolvent enhances the enzymatic ligation.

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