Towards Reversible Localized DNA Hybridization Chain Reactions
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Abstract
Structural and computational DNA nanotechnology has demonstrated enormous progress in the past decade. The development of folding technique such as DNA origami and DNA tiles has enabled construction of many intricate nanoscale objects. Additionally, development of scalable computational technique such as seesaw circuits can facilitate in forming more intelligent nanoscale devices. The ability to create stable platforms for performing complex self-assembly reactions such as molecular walkers and payload transfer reactions, has been resulted from the stable folding techniques. Previously, these molecular reactions were performed in solution without any available platform or designed nanotrack. Thus, the rate of reaction was fundamentally limited to diffusion of reactants. This was one of the reasons for slow computational time even though self-assembly process has an inherent advantage of parallelism.

Recently, DNA hybridization chain reaction, performed on a nanotrack, demonstrated a speed-up of 6 times which gives an idea of the tremendous potential of localization [1]. Not only does localization increase the reaction rate, but it can also improve reaction scalability because of domain reuse. In this work, our goal is to take a step further by reversing these localized computations. As a platform, we use double crossover (DX) DNA tiles nano-track with some DNA overhangs which can be used to attach nucleic acid hairpins. The track is designed to keep hairpins in close proximity to facilitate localized chain reactions. The reversible part of circuit will allow hairpins to restore. In particular, after the reaction is initiated, the input strand is extracted and hairpins are restored, consecutively, to their original state. To observe speed-up and reaction rate, we use multiple techniques such as atomic force microscopy (AFM), ensemble fluorescence spectroscopy and single-molecule imaging.

Localized chain reaction

Figure 1: Localized DNA chain reaction on a DNA track (or DNA origami). Initiator strand diffuses and opens the first hairpin to initiate the computation. This hairpins then opens the other hairpins downstream. Once the final hairpin is open, a reporter complex diffuses to report the reaction completion.

Figure 2: Experimental results of localized DNA hybridization reactions demonstrating speed-up. A direct comparison between fluorescence data of solution-based and localized system demonstrate a drastic reduction in half-time for reaction completion. To further demonstrate reaction completion total internal reflection microscopy (TIRFM) was used to observe localized reactions after attaching DNA origami on glass slides. Scale bars in TIRF images are 1 μm.

Modelling results

Figure 4: Direct comparison of experimental data and data simulated from the model for renewable seesaw motif and OR gate made using renewable seesaw motif [2]. To achieve the best fit, we ran a maximum likelihood estimation (MLE) on experimental data.

Localized reversible computation

To address the problem of leak, cross-talk and scalability, we localize our system on nanostructure such as DNA origami or DX DNA tiles.

1. Localize the entire circuit on a nanostructure. In this case, extractors are sequestered initially and after adding a initiator they are exposed to perform reversal. Once the reversal is complete a complementary strand will sequester extractors again.
2. Localize input with input extractor and fuel with fuel extractor. This will also avert the problem of cross-talk.

Acknowledgement
This work was supported by NSF CCF1617791 and also by Missions & Cultural Representation Sector, Ministry of Higher Education, Egypt.

References