Enzyme displacement reactions for programmable molecular logic

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Short Abstract — We report a novel method for implementing DNA-based logic gates, by modulating activity of deoxyribozymes via toehold-mediated strand displacement reactions, which we refer to as enzyme displacement. The innate catalytic activity of deoxyribozyme sensor gates allows amplification of low concentrations of input. We detect arbitrary input sequences using straightforward gate structures, enabling rapid development of biomedical assays and in vivo monitoring and control circuits.

Keywords — DNA computation, deoxyribozymes, logic gates, circuit design, signal amplification.

I. INTRODUCTION

Biomolecular computing devices show considerable promise for the integrated detection, analysis and processing of signals from the chemical environment, which has applications in directed nanoscale assembly [1] and actuation [2], and autonomous theranostics [3]. A key component in such systems is signal amplification, which allows small input concentrations to generate sizable output signals, as well as reversing signal degradation.

II. RESULTS

Here we report a simple scheme for implementing logic operations using inherently catalytic deoxyribozymes controlled by toehold-mediated strand displacement reactions, which we call enzyme displacement reactions. DNA strand displacement is a robust, well-characterized method for programming reaction pathways in biomolecular computing devices [4]. The use of toeholds as nucleation sites for the interaction [5] allows hybridization and subsequent branch migration reactions to be programmed based on sequence. With a judicious choice of toehold lengths, the reaction can be biased in a particular direction based on thermodynamic considerations [6] without relying on concentration-driven effects. While circuits based solely on hybridization and strand displacement are known to exhibit signal amplification capabilities [6,7,8], this comes at the expense of design complexity. Therefore it is desirable to combine strand displacement techniques with functional oligonucleotides possessing inherent catalytic ability. One such class is the deoxyribozymes [9], single strands of DNA that can catalyze a variety of chemical reactions [10,11].

We report logic gates that combine programmable strand displacement reactions with known deoxyribozymes to produce programmable sensor gates that implement logic functions with inherent signal amplification capability. The entropy-driven activation reaction removes any concentration effects in the activation process. Enzyme displacement gates can be straightforwardly designed to detect arbitrary input sequences and perform well even in the presence of excess concentrations of background DNA.

III. CONCLUSION

Our approach has applications in biomedical assay and sensor development: isothermal, non-protein based approaches are highly desirable for low cost field assays. Deoxyribozymes are known to function in cellular environments [12], and enzyme displacement gates are ideal for the development of synthetic deoxyribozyme-based systems for the observation and control of gene expression in cells. The programmability of biomolecular reactions also enables the development of circuits tailored to monitor specific genes of interest, for purely scientific purposes.

REFERENCES