

Invited Tutorial

Computational design of DNA strand displacement systems

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Molecular devices made of nucleic acids show great potential for biotechnology applications, ranging from the biofabrication of chemical compounds and materials, to the development of high-precision biosensors and intelligent nanomedicine. Such devices can perform complex computation at the molecular scale, while also interfacing directly with the molecular components of living systems. Crucially, they are highly programmable, in that the interactions between nucleic acid strands can be precisely controlled by modifying their nucleotide sequences. DNA strand displacement has recently been proposed as a promising approach for programming computation in nucleic acids, and relies on the hybridization of DNA strands with partial or full complementarity, resulting in the displacement of one or more pre-hybridized strands. Recent work has shown that DNA strand displacement can in principle be used to implement a broad range of computations, including any behaviour that can be expressed as a chemical reaction network. However, designing systems that behave as intended in a biological context is a major challenge, due to high system complexity and the potential for unwanted interference between molecular components. To help address this challenge, we have developed a DNA strand displacement language (Visual DSD) for designing and simulating computational devices made of DNA. The language is a first step towards the development of computational design tools for DNA strand displacement systems.

This tutorial presents an introduction to DNA strand displacement systems, through a collection of simple examples shown in Visual DSD. I will present a number of computational methods that have been developed to model, simulate and analyse these systems, and will illustrate these methods through a series of software demonstrations. The methods include Bayesian inference of kinetic parameters from experimental data, modular proofs of behavioural equivalence, symbolic verification of the functions computed by strand displacement systems, and probabilistic model-checking. I will also illustrate different types of strand displacement systems that can be constructed experimentally, including well-mixed systems consisting of large numbers of strands in solution, spatially organised systems in which strands are allowed to diffuse, and systems with topological constraints in which strands are tethered to a surface. These examples illustrate the breadth of systems that can be designed with DNA, while also highlighting the many challenges that still remain in order to verify such systems.