Toward electronically-functional, self-assembling DNA nanostructures

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Recent work has demonstrated that DNA, ordinarily considered a weak conductor, can be functionalized to carry electronic charge by site-specific incorporation of single silver ions inside the double helix via the non-canonical pairing of mismatched cytosines through Ag^+ coordination: (dC:Ag^+:dC) [1,2]. Through the alteration of sequence composition and cation availability, a variety of nanowires can be synthesized with tuneable length, ion distribution, and uniformity. These wires are more thermostable than Watson-Crick DNA, can shield intercalated Ag^+ from aqueous solvents, and are able to form in the absence of cluster contamination. We use computational sequence design algorithms to introduce nonlinear geometry to these nanowires, with the goal of creating self-assembling DNA nanostructures that may have potential for neural architectures from electrically-functional oligonucleotide components.

1. LINEAR NANOWIRES

The introduction of Ag^+-coordinated sequence mismatches between opposing cytosine nucleobases does not significantly perturb the b-form helix of DNA [3]; and even in short, 11-mer polycytosines, this bond is able to withstand temperatures exceeding 90 ^{0}C, avoid reduction by aqueous agents, and outcompete precipitants for Ag^+. With careful buffer preparation, robust DNA nanowires can be produced for potential single-molecule electronic applications. Excess supply of Ag^+ during annealing can affect the overall length of nanowires when sequences are designed to be promiscuous (e.g., through high cytosine density), while enzymatic end-end ligation can extend these wires up to ~100 nm in length. With a molecular conductance ~$10^{-3}G_0$, this linear species is an attractive candidate for integration into devices or networks.

2. BRANCHED STRUCTURES

Synthesis of DNA nanostructures that contain dC:Ag^+:dC base pairs effectively changes the chemical language of assembly used to drive structure formation. As such, we have assayed a variety of nanostructures that require minimal-length oligomers in order to reduce the thermodynamic constraints that emerge from base pair promiscuity. We have explored several structures, including T-junction lattices based on the work of Hamada et al [4] (Figure 1), as well as Holliday junction and double crossover junction units based on foundational work from the Seeman group [5,6]. We explore the differences between rigid and flexible tiles using atomic force microscopy in both fluid and air, and suggest methods for the optimization of future structure design and assembly.

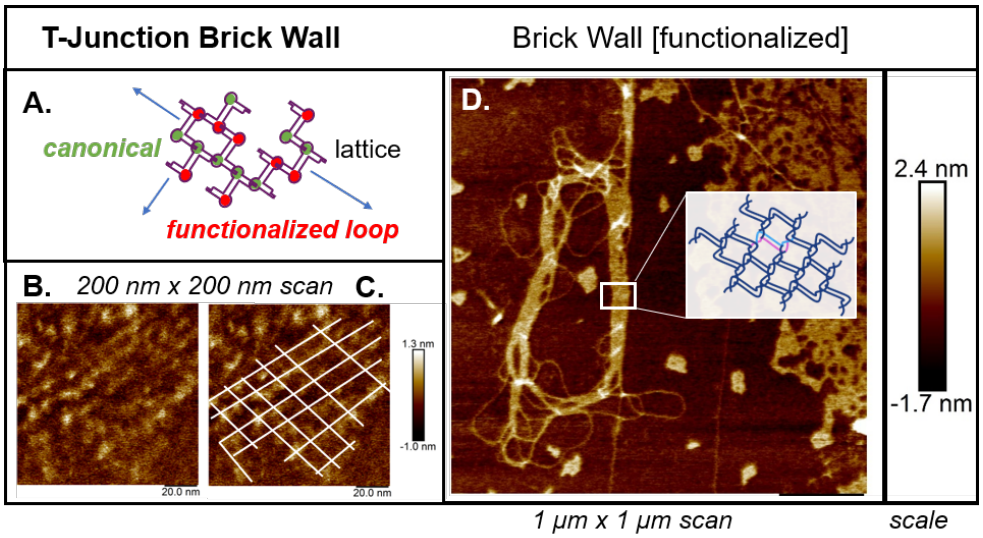

Figure 1. Formation of a brick wall structure based on [4]. **A)** T-junction tiles are small units that bind using sticky ends and hairpin loops. **B)** This structure was imaged using high-resolution AFM and **C)** was shown to agree with the predicted lattice shape. **D)** Larger networks were observed, but the flexibility of the unit may preclude defect-free assembly at the micron scale.

3. Computational Sequence Design

The addition of the dC:Ag^{+}:dC base pair changes the lexicon of DNA assembly and drastically increases the likelihood of thermodynamic promiscuity among the nucleobases during structure formation. In order to drive accurate structure formation, we have developed a suite of software tools for the iterative optimization of DNA sequences with arbitrary pairing rules, editable geometry, and customizable local parameters. We designed a genetic algorithm to evolve solutions to this complex thermodynamic landscape *in silico* using a vectorized approach to heterostructure analysis. We present results based on this model, and we suggest a mathematical basis for dimer analysis for future applications.

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