Computational Elucidation of the Self-Assembly of Nucleic Acids into Novel Materials

Stacy SNYDER and Yaroslava YINGLING
Materials Science and Engineering, North Carolina State University
Raleigh, NC 27695, USA

Nucleic acids, such as RNA and DNA molecules, are especially appealing for nanobiotechnological applications due to their versatility in function and structure and molecular recognition properties of base pairing. Using these properties, DNA and RNA molecules have been engineered into novel nanostructures to make effective 2D and 3D nanoparticles, nanotubes, drug delivery capsules, and scaffolds for the assembly of molecules or electronic components. We investigate the self-assembly of nucleic acids into thin, multilayered films, which have been prepared using single-stranded DNA deposited via a layer-by-layer technique [1]. These thin films can form novel hollow multilayer capsules that posses unique engineered features such as size, shape, composition, porosity, stability, surface functionality, and biodegradability [2].

DNA films constructed with the layer-by-layer technique use DNA hybridization in place of electrostatics used in the more common polyelectrolyte charge-alternating structures. DNA films are assembled on a base layer such as polyT_{30}, with additional layers of oligonucleotides having a diblock structure which allows both hybridization with the existing film and a nonhybridizing tail for hybridization of the subsequent layer.

The effects of nucleic acid strand length, nucleotide sequence, and the number of layers on film growth and structure are studied. Molecular dynamics simulations are performed using Amber 9 with the ff99 Cornell force field for nucleic acids. Implicit solvent (Generalized Born approximation) is used with 0.1M salt concentration. The initial distance between strands corresponds to crystallographic parameters for DNA helices, and the bases of the helices are constrained with a harmonic force to represent the effect of the infinite DNA film. Figure 1 shows a snapshot from a simulation of neighboring 40mer strands.

We monitor the dynamics and conformation of successive DNA oligonucleotides as a film is grown in order to explain experimental results, including anomalous changes in growth efficiency with strand length. A minimum oligonucleotide length of approximately 20 nucleotides is required for film growth, due to the increased probability of self-hybridization and triple helix structures for shorter strands. Insight into the observed decrease in growth efficiency for 60-mer strands is gained by monitoring the probability of crossover or hybridization of neighboring strands in the film. Clearer understanding of the self-assembly process is expected to make possible the algorithmic self-assembly of nucleic acid thin films for applications in drug delivery and biological sensing.

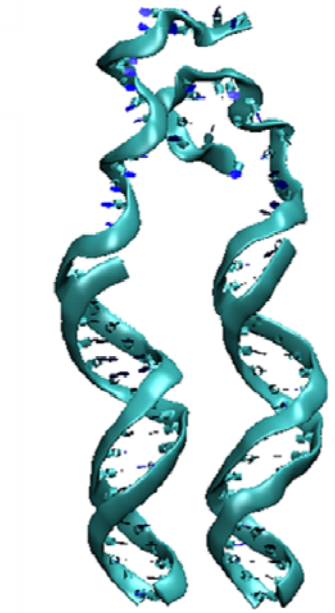

Figure 1. Simulation showing neighboring 40mer strands.

[1] A.P.R. Johnston, H. Mitomo, E.S. Read, and F. Caruso, “Compositional and Structural Engineering of DNA Multilayer Films”, **Langmuir**, Vol. 22, No. 7, 2006, pp.3251-3258.

[2] A.P.R. Johnston, E. S. Read, F. Caruso, "DNA Multilayer Films on Planar and Colloidal Supports: Sequential Assembly of Like-Charged Polyelectrolytes", **Nano Letters**, Vol 5, No. 5, 2005, pp. 953-956.