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COSM force field: computer-aided design tool for DNA origami

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DNA origami technique enables construction of sophisticated nanoscale structures based on folding of single-stranded 'scaffold' DNA with set of 'staple' oligonucleotides[1]. Programmable shape of origami objects is used for diverse applications in biology, chemistry and materials: for the directional drug delivery, the single-molecule study of chemical reactions, as a substrate for nanoelectronic circuitry etc. Experimental validation of target structures is time-consuming and cost-intensive, so prediction of their shape and stability could contribute to creating more intricate and reliable structures.

The main design tool for DNA origami structures is software called cadnano[2]. Cadnano origami scheme consists of linearly aligned double-helical DNA domains with the specified length and mutual arrangement in the hexagonal or square lattice. However, the most origami constructions have sophisticated third-dimensional structure often with the presence of flexible elements, so it is necessary to develop a new tool for rapid and reliable testing of mobility and folding efficiency of such structures.

At the moment, there is only one tool of this kind – CanDo[3]. It represents a double-stranded DNA as an elastic rod with specified geometrical and material parameters and is not able to simulate single-stranded parts of structures, which are often crucial for successful origami folding. This fact significantly limits the applicability of this approach for intricate three-dimensional structures.

To make cadnano schemes useful for origami modeling, we developed converter from cadnano output format to pdb coordinates considering DNA sequence, force field COSM (Coarse-grained Origami Structures Modeling) for DNA origami simulation using molecular dynamics package GROMACS and converters from cadnano scheme to COSM-model and from COSM to full-atom structure. COSM force field is adjusted for simulations in vacuum, so system size is significantly smaller on account of the absence of solvent. COSM is based on the coarse-grained DNA model with (according to the chosen lattice) 17 or 19 particles types corresponding different types of origami substructure. The number of particles in the final system is reduced from millions in full-atom models to hundreds in COSM, what makes the calculations many times faster.

COSM model accuracy has been tested on small (400 bp) structures experimentally and using coarse-grained and full-atom molecular dynamics and on large (3200-12000 bp) structures by comparing with published TEM micrographs. In the future we are planning to create a web-service able to perform DNA origami simulation using COSM.

Литература

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