8th. World Congress on Computational Mechanics (WCCM8)
5th. European Congress on Computational Methods in Applied Sciences and Engineering (ECCOMAS 2008)
June 30 – July 5, 2008
Venice, Italy

THERMODYNAMIC AND MECHANICAL PROPERTIES OF SIMPLE RNA NANOSTRUCTURES

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Key Words: RNA nanostructures, RNA architectonics, RNA thermodynamics, RNA dynamics, mesoscopic models.

ABSTRACT

In recent years, significant progress in the understanding of the RNA structure led to the emergence of the "RNA architectonics" – a set of recipes for (self-)assembly of the RNA nanostructures of the arbitrary size and shape [1,2]. Smallest RNA building blocks - "tectorRNAs", typically bearing well-defined structural features (e.g. angles), such as "right angle motif" [1], 'kink-turn motif' [2,3] or "RNAIi/RNAIIi kissing loop complex" [4] were manipulated (either experimentally [1,2] or via computer simulation [4]) into the desired 2D or 3D nanostructures (squares, hexagons, cubes, tetrahedrons etc) that can be further assembled into periodic or quasiperiodic lattices.

In this study, we analyze the thermal dynamics, as well as the response to an applied external force of several such building blocks, focusing on square- and hexagon-shaped cyclic RNA nanostructures. While certain data about thermal stability of such nanostructures are already available [1,2,4,5], both from the experiments and the simulations, a much deeper and detailed understanding of their stability and dynamics is needed. In particular, one of the main emphases of this work is on the effect of the counterions, that may affect strongly the behavior of e.g. the kissing-loops structural motifs [8]. Another emphasis of the present study is on the understanding of the response of the forementioned nanostructures to an applied external force, an important factor in the context of a range of promising applications, including RNA nanostructures in the man-made molecular machines.

Compared to the DNA, nanostructures of which have been extensively studied before, the RNA as a nano-engineering material brings several additional challenging features. Firstly, due to the specificity of the interactions in RNA (such as noticeable presence of the non-Watson-Crick base pairing) it shows much larger structural modularity and diversity of the tertiary structural building blocks, ~200 versus ~20 for DNA [2]. Secondly, the RNA nanostructures are often much more conformationally flexible that the DNA ones, which makes them very promising in applications. Indeed, an interesting

conformational dynamics (strongly mediated by the presence of water and counterions) of some of the simple structural RNA units has already been reported [5, p. 320].

We present all-atom classical Molecular Dynamics results on the stablity and fluctuational and conformational dynamics of several simple RNA cyclic nanostructures. Firstly, the landscape for nearest metastable ("inherent") structures is seached for and the pathways for melting as well as the final configurations are identified. Secondly, the stablity and the dynamics of the nanostructures under the action of an applied external force is studied. In particular, several computational results will be presented, demostrating the role of salt counterions on the behavior of different RNA nanostructures.

The data obtained in the full MD simulations are used as an input for a simplified mesoscopic model developed on the basis of the PBD, Go and SOP models [6,7], where the nucleotides are represented by the interaction centres and the effective interactions between them are tweaked in the way to fit the nanostructures atomic connectivity, thermal and mechanical properties (among other things, we will provide details of our attempt to take the roles of the counterions and kissing loops into account). Finally, the dynamics of such a simplified model is further investigated and the results demostrating the nonlinear hysteretic behavior under the combined action of the external mechanical force and the temperature will be presented.

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