

Kinetics of the long single - stranded RNA: nonequilibrium steady state

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The event of single-stranded (ss) nucleic acids hybridization is a key process in any DNA or RNA sensor activity and in many molecular biology techniques such as polymerase chain reaction (PCR), *in situ* hybridization, etc. Two types of conformational rearrangements in RNA are possible: rearrangement of the secondary structure with characteristic time scale τ_2 and tertiary structure fluctuations with characteristic time scale τ_3 . The difference between timescales τ_2 and τ_3 is well-pronounced. The following mental experiment has been considered [1,2]. The ssRNA molecule is dissolved initially in the solvent at temperature T' which satisfies inequalities $\Theta < T' < T_m$, where T_m is the melting temperature and Θ is the Flory temperature. Under these conditions the RNA molecule is a random coil with a well defined secondary structure. Next, transfer a very small amount of our RNA containing solution into the same kind of solvent but with temperature T , such that $T < \Theta$. Now the content of the secondary and tertiary structures does not correspond to the temperature of the thermostat, and the system appears in a non-equilibrium state. In the beginning, the secondary and spatial structures in this state still correspond to the temperature T' but they start to relax to the new temperature T . At the end of the process, the RNA will arrive at a compact globular state with some secondary structure pattern. On the timescale τ , such that $\tau_3 \ll \tau \ll \tau_2$, the secondary structure and spatial arrangement of the effective monomers (non-paired regions) are not in thermal equilibrium, and this stationary non-equilibrium steady state can be described in terms of the effective partition function [3]. The replica technique method was applied to address the non-equilibrium steady state of the coarse-grained model for the RNA molecule. A non-equilibrium phase transition of second order between the glassy phase and the ensemble of freely fluctuating structures has been observed. The non-equilibrium steady state is investigated as well and the thermodynamic characteristics of the system have been evaluated. The non-equilibrium behavior of the specific heat is discussed. Based on our analysis, we point out the state in the kinetic pathway in which the RNA molecule is most prone to hybridization.

[1] Y. Mamasakhlisov, et al., Europhys. Lett. **106**, 48007 (2014).

[2] Y. Mamasakhlisov, et al., Europhys. J. E **38**, 100 (2015).

[3] V. Dotsenko, et al., J. Phys. A **27**, 2351 (1994).