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Physics

DIFFERENT STABILITY OF RNA SECONDARY AND TERTIARY STRUCTURES

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The goal of this article is to clarify contribution of the chain entropy in stability of RNA secondary and tertiary structures. The Hamiltonian of the model includes relevant interactions explicitly. We show that different stability of secondary and tertiary structures governed by chain entropy rather than energy of interaction.

***Keywords*:** RNA, folding, entropy.

The RNA molecule has a remarkably versatile role in cellular processes [1–4]. The main focus of the given article is the interplay between the secondary and tertiary structures of RNA molecule. We examine the behavior of a RNA-like molecule using the approach, developed recently in [5]. The melting behavior, obtained in the framework of our model, is in a qualitative agreement with experimental data [6].

The Model and Theory. We describe the RNA molecule with N monomers by a random Gaussian chain, in which electrically charged “beads”, representing the mononucleotides, are connected with elastic “springs”. The monomers are enumerated from 1 to N. The structure of the molecule is described by introducing two $N\times N$ matrices: I – the complementarity matrix $\widehat{M}=|M_{ij}|$, where $M_{ij}=1$, if the i-th and j-th bases are complementary (Watson-Crick type), and $M_{ij}=0$ otherwise; II – the contact matrix $\widehat{C}=|C_{ij}|$, where $C_{ij}=1$, if the i-th and j-th bases are hydrogen-bonded, and $C_{ij}=0$ otherwise. Thus, the base pair (i, j) contributes to the secondary or tertiary structure only if $M_{ij}C_{ij}=1$. The spatial configuration of the chain is defined by the set $\{\mathbf{r}_i\}_{i=1,2,\dots,N}$ of the radius-vectors of the monomers. Hereafter the bold roman letters indicate space vectors. The Hamiltonian of the model reads

$$H\{\mathbf{r},\widehat{C},\widehat{M}\}=H_{el.}(\mathbf{r})+H_{rep.}(\mathbf{r})-e\sum_{i<j=2}^{N}M_{ij}C_{ij}+\sum_{i<j=2}^{N}M_{ij}C_{ij}\frac{3T(\mathbf{r}_i-\mathbf{r}_j)^2}{2d^2}, \quad (1)$$

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where T is the temperature, δ is the linear size of the Watson-Crick base pair, $\varepsilon > 0$ is the base pair stabilization energy. In (1) the term

$$H_{el.}(\mathbf{r}) = \frac{3T}{2a^2}\sum_{i=1}^{N}(\mathbf{r}_i - \mathbf{r}_{i+1})^2 \qquad (2)$$

describes the energy due to polymeric elasticity with a being the length of the Kuhn segment of the chain.

The term $H_{rep.}(\mathbf{r})$ in Hamiltonian (1) describes the role of the electrostatic repulsion explicitly [7, 8] as

$$H_{rep.}(\mathbf{r}) = l_B f^2 r_D^2 \sum_{i \neq j} \delta(\mathbf{r}_i - \mathbf{r}_j), \qquad (3)$$

where l_B is the Bjorrum length, f is the partial charge per monomer, and r_D is the Debye screening length.

In the case of spatially uniform monomer density ρ one obtains

$$\beta H_{rep.}(\rho) = l_B f^2 r_D^2 N \rho, \qquad (4)$$

where $\beta = 1/T$, $\rho = N/V$, and V is the volume, occupied by macromolecule.

The third term in (1) describes the energy of saturated hydrogen-bond interactions. Using the replica approach [9] and the one-step replica breaking scheme [10], variational free energy for any integer number n can be calculated [5].

Freezing and Melting Transitions. Below the freezing temperature the configurational space of the molecule is drastically reduced. Instead of exponentially large numbers of conformations, now the state of the molecule is dominated by only a few low-energy conformations. The molecule is found in the frozen state [10, 11]. We get the freezing temperature as

$$\frac{\varepsilon}{T_{fr.}} = \ln\omega - 2\ln\left(1 - \frac{2S}{\omega}\right), \qquad (5)$$

where S is the entropy loss per monomer, caused by chain freezing, and $\omega = 2 l_B f^2 r_D^2 \delta^{-3}$.

The basic experimentally measurable quantity, describing RNA secondary structure, is the degree of helicity θ, which is defined as the average fraction of the hydrogen-bonded base pairs:

$$\theta = \frac{2}{N}\left\langle \sum_{i<j} M_{ij} C_{ij} \right\rangle. \qquad (6)$$

Using Equation (6) we obtain

$$\theta = 1 - \frac{1}{2} z \sqrt{\omega}, \qquad (7)$$

where $z = e^{-\beta\varepsilon/2}$.

The measure of stability of the secondary structure is so called “melting temperature” T_m, defined as the point, where $\theta = 1/2$. By substituting this value in (7), one finds

$$T_m = \frac{\varepsilon}{\ln\omega}. \qquad (8)$$

Combining with equation (5), we obtain $T_{fr.} < T_m$ and

$$\frac{\varepsilon}{T_{fr.}} - \frac{\varepsilon}{T_m} = -2\ln\left(1 - \frac{2S}{\omega}\right) > 0 . \qquad (9)$$

The stability difference between the secondary and tertiary structures is usually explained by lower free energy of base pair formation in comparison with more weak tertiary contacts. Our consideration suggests that for the different stability of tertiary and secondary structures the entropy S necessary for 3*D* structure formation is also responsible.

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ՌՆԹ-ի երկրորդային և երրորդային կառուցվածքների տարբեր կայունություններ

Աշխատանքի նպատակն է ՌՆԹ-ի երկրորդային և երրորդային կառուցվածքների կայունության մեջ շղթայի էնտրոպիայի ներդրման որո-շումը: Առաջարկված է մոդել հիմնական փոխազդեցությունները բացա-հայտ կերպով ներառող համիլտոնիանով: Ցույց է տրված, որ երկրոր-դային և երրորդային կառուցվածքների տարբեր կայունություններ որոշվում են ավելի շատ շղթայի էնտրոպիայով, քան փոխազդեցության էներգիայով:

Различная стабильность вторичной и третичной структур РНК

Целью данной работы является определение вклада энтропии цепи в стабильность вторичной и третичной структур РНК. Предложена модель с гамильтонианом, в явном виде включающем основные взаимодействия. Показано, что различная стабильность вторичной и третичной структур определяется скорее энтропией цепи, нежели энергией взаимодействия.