

Effect of Correlations in the Interaction along Polymer Chain on the Globule Structure

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Abstract—A special potential for interaction between polymer chain units, whose energy decreases with increasing distance s between the units as s^{-1} , was introduced for the first time. According to Monte Carlo simulation, interactions of this type result in the formation of a globule with an equilibrium packing of domains in space. The radius of gyration of a chain segment in these globules varies with segment length according to the scaling law typical of crumpled globules.

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It is known that upon fast cooling, a macromolecule is collapsed in two stages: first, so-called crumpled globule is formed [1, 2] in which successive chain segments are assembled into dense clusters separated from one another, then the boundaries between the clusters are diffused, chain segments are mixed, chain ends reptate through the globule bulk, and an equilibrium globule is formed.

The formation of a crumpled globule is related to the kinetics of fast compacting of the molecule where adjacent chain segments are first combined into dense blobs, “first-level crumples,” then adjacent first-level blobs form second-level blobs, and so on up to the formation of a globule with the maximum packing density of monomer units; the radius of gyration R_g of the globule depends on the number N of monomer units in the chain as $R_g(N) \sim N^{1/3}$. A characteristic feature of the crumpled globule is that shorter chain segments of length s ($s < N^{2/3}$) obey the same scaling relation $r_g(s) \sim s^{1/3}$ as the whole macromolecule, whereas for the equilibrium globule, $r_g(s) \sim s^{1/2}$. In this respect, the crumpled globule has a self-similar (hierarchical) packing and is fractal. One more feature of a fractal globule is the domain type of packing of units; there-

fore, the probability of local contacts p_c between segments along the chain decreases as $p_c \sim s^{-1}$, which is more slowly than for the equilibrium globule, $p_c \sim s^{-3/2}$. Conformations possessing this type of properties were actually detected by Hi-C analysis of the spatial packing of chromatin [3].

There are various methods for simulation of crumpled structures in computer experiments: “sticky” random walk [4], fast collapse in a compressing field [3, 5, 6], and fractal structure specification based on Hilbert curves [4, 7]. It was shown that fractal-like structures can arise in confined space upon compacting of amphiphilic macromolecules [8]. The hierarchical collapse models, resulting in crumpled structures were also constructed on the basis of special “hierarchical” potential [9] and drop coalescence [10].

Computer simulations demonstrated that the domain globular structure in homopolymer chains is destroyed rather rapidly with relaxation [7, 11]. This takes place both in the case where the fractal globule has been formed upon the collapse of a macromolecule and in the cases where fractal conformations were specified in a special way using the Hilbert curves [7, 11].

In nature, the domain structure of the globule is caused by heterogeneous composition of the macromolecule, selectivity of interaction of chain units with one another, unit sequence details, and so on. It can be reasonably suggested that the sequence of macromolecule units that form the equilibrium domain globules is such that interactions between the units adjacent along the chain are compensatorily the strongest and the interaction strength declines with increasing distance along the chain. It is clear that in the general

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case, the law of interaction is sophisticated, being dependent on the detailed structure of the units, position of a unit in the chain, and details of the unit environment; generally speaking, each pair of monomer units can have its own interaction potential. However, in the simplest case, the attraction energy can be assumed to decrease with increasing distance along the chain as $1/s$, like the probability of contact between the units in the fractal globules.

The purpose of this work is to study the conformation properties of macromolecules whose units are subjected to a potential the strength of which depends on the distance between the units along the chain.

MODEL AND SIMULATION TECHNIQUE

The investigation was performed by the Monte Carlo method within the framework of the continuum model of the polymer chain. Each monomer unit is a rigid sphere with the diameter $d = 1$ (this is unit length in the model), the bond length between the adjacent units along the chain can freely fluctuate in the range $0.8 < L_{\text{bond}} < 1.25$ (that is, the units can partly overlap). The potential of non-valent interactions between the monomer units that do not adjoin each other along the chain is specified as

$$U_{ij} = \begin{cases} \infty, & r_{ij} < 1, \\ -\varepsilon \left(1 + \frac{A}{B + s_{ij}} \right), & 1 \leq r_{ij} \leq R_{\text{cut}}, \\ 0, & r_{ij} > R_{\text{cut}}, \end{cases}$$

where r_{ij} is the distance between two units i and j in space, s_{ij} is the distance between the same units along the chain measured as the number of bonds, R_{cut} is the potential cutoff radius, ε is an energy parameter, and A and B are dimensionless parameters. This potential consists of a potential well $U_{\text{const}} = -\varepsilon$ corresponding to the solvent quality and a component depending on the distance s along the chain as $\frac{A}{B+s}$. This corresponds to the well-known bead-spring model [12, 13], but with a simple geometric (without elastic potential) bond length constraint and with a component depending on the distance along the chain.

The simulation was carried out by the Monte Carlo method. An elementary step of the simulation was an attempt to shift a randomly chosen unit by a random vector whose projection on each axis did not exceed 0.1 in absolute magnitude. The steps that did not violate the excluded volume condition and the bond length condition were accepted according to the Metropolis criterion; i.e., the probability that a trial move is accepted is given by $P_{\text{acc}} = \min(1, \exp(-\Delta E/k_B T))$, where ΔE is the change in the system energy upon the test shift, k_B is the Boltzmann constant, and T is tem-

perature. Each Monte Carlo step (MCS) comprises N test elementary steps.

In what follows, the potential with a non-zero s -dependent component will be called special ($A \neq 0$). The potential without the additional component ($A = 0$) will be called normal.

The initial state was generated as self-avoiding random walk. The chain collapse was performed by gradual increase in $\varepsilon/k_B T$ by 0.05 every 5×10^7 MCSs. The data obtained for each $\varepsilon/k_B T$ were averaged every 10^4 MCSs and over several implementations with different initial conformations.

Relatively short chains with the degree of polymerization $N = 64, 128, \text{ and } 256$ and longer chains ($N = 1024$) were considered. In the former case, the following parameters were chosen: $A = 32, B = 8, R_{\text{cut}} = 1.5$, while in the latter case, $A = 140, B = 35, R_{\text{cut}} = 2.0$. In both cases, if the units were spaced by a distance shorter than the cutoff radius, it was taken that for monomers infinitely remote along the chain, $U_{ij} = -\varepsilon$, and for monomers proximate along the chain ($s_{ij} = 2$), $U_{ij} \sim -4.2\varepsilon$ in the former case and $U_{ij} \sim -4.8\varepsilon$ in the latter case.

The globules obtained in this way were additionally equilibrated using a "mixing" algorithm consisting in the following. In the first stage, a harmonic potential on the bond length was added, $U = k_{\text{el}}(L - L_0)^2$, $k_{\text{el}} = 50k_B T$, with the equilibrium bond length $L_0 = 2$ much exceeding the bond length in the initial model, thus enabling free self-intersection for the chain. The type of bulk interaction potential remained the same (normal/special), and the temperature was selected in such a way that the chain did not turn into a coil upon sharp increase in the bond length. Then the equilibrium bond length L_0 was decreased by $\Delta L = 0.02$ every 800 000 MCSs until the maximum bond length was less than 1.25 (constraints of the initial model).

RESULTS

Figure 1 shows the dependences of the radius of gyration R_g of the macromolecule on $\varepsilon/k_B T$. It can be seen that as the temperature is lowered, the radius of gyration decreases. In the case of normal potential (Fig. 1a), the plots $R_g(\varepsilon/k_B T)$ can be approximated by an S-shaped curve; the plots R_g^2/N intersect in the θ point located in the range $0.36 < \varepsilon/k_B T < 0.39$. At this point, the macromolecule is known to be a Gaussian coil ($R_g \sim N^{1/2}$) [14].

With the special potential (Fig. 1b), the plot $R_g^2(\varepsilon/k_B T)$ does not have a visible inflection point, the minimum R_g value being achieved at much higher temperature than in the case of normal potential; the plots R_g^2/N intersect when the macromolecules have

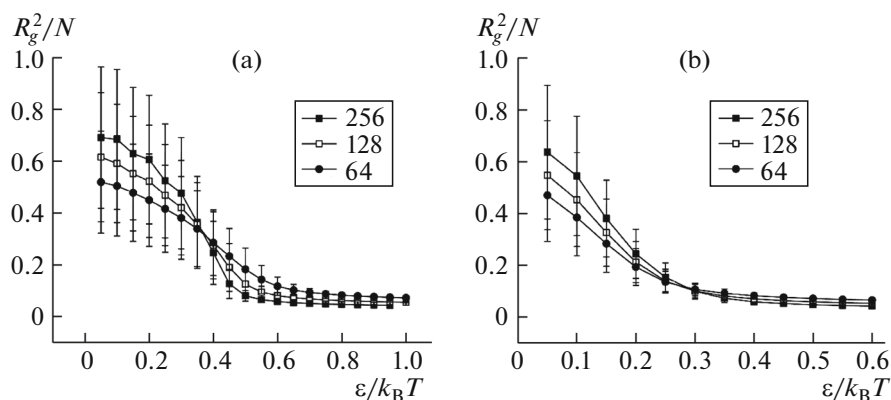


Fig. 1. Dependences of R_g^2/N on $\varepsilon/k_B T$ for various chain lengths N for (a) normal and (b) special potential.

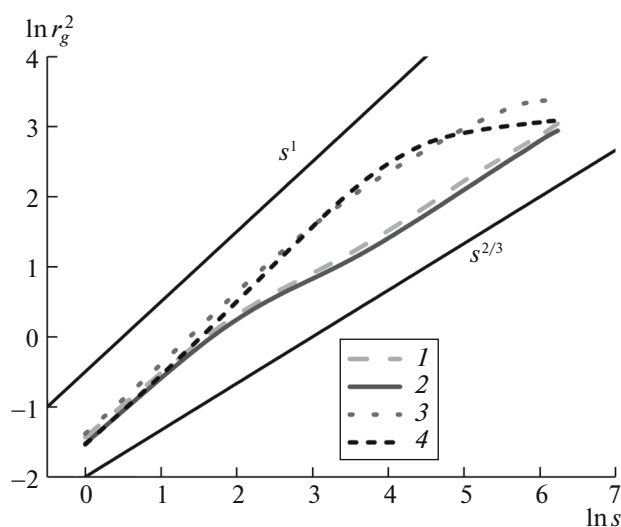


Fig. 2. Squared radius of gyration vs. subchain length s in logarithmic coordinates for the chain $N = 1024$.

almost reached their minimum size and are actually rather dense.

Figure 2 shows the variation of the squared radius of gyration r_g^2 of a subchain plotted vs. the subchain length s in a globule with normal (3, 4) and special (1, 2) potential immediately after the collapse (1, 3) and after “mixing” procedure (2, 4). In the case of normal potential (according to earlier results, see, e.g., [6]), the plot $r_g^2(s)$ has a rather extended region where $r_g^2(s) \sim s$ and the subchain is Gaussian. After mixing, additional equilibration takes place, the plot $r_g^2(s)$ changes, and the Gaussian statistics ($r_g^2(s) \sim s$) is observed in a greater range of s . In the globules formed under the action of the special potential, the plots

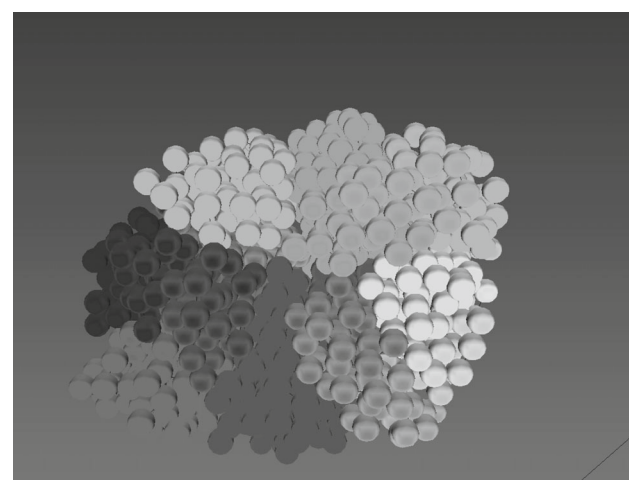


Fig. 3. Snapshot of a low-energy globular conformation for a homopolymer composed of $N = 1024$ units for the special potential model. Gradient coloring along the chain is used (the monomers proximate along the chain are of the same color and those remote along the chain are of different colors).

$r_g^2(s)$ before and after mixing coincide, the dependence for $40 < s < 512$ being described by a power law $r_g^2(s) \sim s^{0.7}$, which rather corresponds to a fractal ($s^{2/3}$) than to an equilibrium (s^1) globule.

Figure 3 shows a snapshot of the globule formed under the special potential with gradient coloring of the units along the chain. The globule is seen to have a cluster structure, the monomer units proximate along the chain being combined into domains, which are spatially separated from other chain regions. Note that the cluster structure of this type is a typical feature of fractal (crumpled) globules [6]. It should be noted, however, that the globule shape is generally non-spherical.

Thus, conditions were elucidated that favor the formation of stable globular domain conformations in

which the radius of gyration of a chain segment varies with the segment length according to the scaling law inherent in crumpled globules. More detailed investigations are planned for the near future.

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REFERENCES

- Grosberg, A.Y., Nechaev, S.K., and Shakhnovich, E.I., *J. Phys.*, 1988, vol. 49, no. 12, pp. 2095–2100.
- Grosberg, A.Y., Rabin, Y., Havlin, S., and Neer, A., *Europhys. Lett.*, 1993, vol. 23, no. 5, pp. 373–378.
- Lieberman-Aiden, E., van Berkum, N.L., Williams, L., Imakaev, M., Ragozcy, T., Telling, A., Amit, I., Lajoie, B.R., Sabo, P.J., Dorschner, M.O., Sandstrom, R., Bernstein, B., Bender, M.A., Groudine, M., Gnirke, A., Stamatoyannopoulos, J., Mirny, L.A., Lander, E.S., and Dekker, J., *Science*, 2009, vol. 326, no. 5950, pp. 289–293.
- Tamm, M.V., Nazarov, L.I., Gavrilov, A.A., and Chertovich, A.V., *Phys. Rev. Lett.*, 2015, vol. 114, no. 17, p. 178102.
- Mirny, L.A., *Chromosome Res.*, 2011, vol. 19, no. 1, pp. 37–51.
- Imakaev, M.V., Tchourine, K.M., Nechaev, S.K., and Mirny, L.A., *Soft Matter*, 2015, vol. 11, no. 4, pp. 665–671.
- Schram, R.D., Barkema, G.T., and Schiessel, H., *J. Chem. Phys.*, 2013, vol. 138, no. 22, p. 224901.
- Glagoleva, A.A., Vasilevskaya, V.V., and Khokhlov, A.R., *Soft Matter*, 2016, vol. 12, no. 23, pp. 5138–5145.
- Avetisov, V.A., Ivanov, V.A., Meshkov, D.A., and Nechaev, S.K., *JETP Lett.*, 2013, vol. 98, no. 4, pp. 242–246.
- Bunin, G. and Kardar, M., *Phys. Rev. Lett.*, 2015, vol. 115, no. 8, p. 088303.
- Chertovich, A. and Kos, P., *J. Chem. Phys.*, 2014, vol. 141, no. 13, p. 134903.
- Gerroff, I., Milchev, A., Binder, K., and Paul, W., *J. Chem. Phys.*, 1993, vol. 98, no. 8, pp. 6526–6539.
- Kremer, K. and Grest, G.S., *J. Chem. Phys.*, 1990, vol. 92, no. 8, pp. 5057–5086.
- Grosberg A.Yu., Khokhlov A.R., *Statisticheskaya fizika makromolekul* (Statistical Physics of Macromolecules), Moscow: Nauka, 1989.
- Sadovnichy, V., Tikhonravov, A., Voevodin, V., and Opanasenko, V., in *Contemporary High Performance Computing: From Petascale toward Exascale*, London: Chapman and Hall/CRC, 2013, pp. 283–308.

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