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Molecular Dispenser: Conformation-Dependent Design Approach

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In this Communication, we propose a new approach to the molecular dispenser and illustrate some features of this system using computer simulation techniques. Our approach is based on the idea of conformation-dependent sequence design of copolymers,[1,2] which includes the generation of a specific primary sequence of an AB copolymer via "coloring" of a homopolymer chain in a certain conformation. In the case when coloring is performed in a globular conformation with the core of the globule and its surface layer colored differently, such copolymers are known as "protein-like" copolymers, and they have significantly different properties as compared to the random or random-block counterparts.[1−4] However, the design of sequences via the "coloring procedure" can be performed not only for a globular conformation. For example, in refs 2 and 5 the notion of adsorption-tuned copolymers was introduced, where the "coloring" procedure was implemented for a homopolymer chain adsorbed on a plane surface.

The idea of a molecular dispenser is a further development in this direction. Namely, we consider the conformation of a homopolymer chain strongly adsorbed on a spherical colloidal particle (Figure 1a) and perform sequence design for this state of macromolecule. The initial motivation behind this design procedure was as follows: if we eliminate the "parent" colloidal particle after the design is completed (e.g., by etching), the resulting copolymer will be hopefully tuned to selectively adsorb another colloidal particle of the parental size. That is, if such a copolymer is exposed to a polydisperse colloidal solution of particles with different size, it will hopefully form a most stable adsorption complex with the particle having the same radius as that under the design conditions (parental conditions).

Our design scheme leading to the molecular dispenser can be described as follows. First, we consider a homopolymer chain attracting to a colloidal particle. The solvent is considered to be poor enough, so there is a certain attraction between monomer units as well. Such a chain can form an adsorption complex with the particle. (A typical conformation obtained in the simulation described below is shown in Figure 1a.) One can see that in the case of sufficiently long chain only part of chain segments is in direct contact with colloidal particle, while other segments form flowerlike loops at equilibrium. Further, we apply the "coloring" procedure in which 50% of the chain segments in the loops are considered as hydrophilic, while the segments located closer to the particle remain hydrophobic; i.e., they conserve attraction to the particle (Figure 1b). Such a "coloring" procedure can be performed via chemical modification of monomer units that are located in the surface layer of the polymer−particle complex, in a manner similar to that described in experimental works.[6] As we will show below, if the design is stopped at this stage, the pronounced selectivity of the complex formation of the resulting macromolecules with colloidal particles is not achieved. However, if a certain number of additional cross-links between hydrophobic units is introduced, thus fixing the cage structure of the central cavity (Figure 1b), the macromolecule emerging after elimination of colloidal particle (Figure 1c) does indeed show the features of a molecular dispenser.

It should be noted that our approach is also stimulated by existing experimental works. In particular, recently, new experimental methods of preparation of nanometer-sized hollow-sphere structures have been suggested[7−9] because of their possible usage for encapsulation of molecules or colloidal particles. The preparation of hollow-sphere structures, generally, is based on self-assembling properties of block copolymers in a selective solvent, i.e., on the formation of polymer micelles with a nanometer-sized diameter. Further cross-linking[7−9] of the shell of the micelle and photodegradation[10] of the core part produce nanometer-sized hollow cross-linked micelles.

The system we examined in our study consists of a single polymer chain and a spherical particle. The polymer was considered as a chain of $N = 512$ monomer units. Each monomer unit (m) is characterized by diameter $\sigma_m = 1$ and mass $m_m = 1$. The bonded monomer units were connected through a FENE potential,[11−13] while the angles between neighboring bonds were not restricted. All nonbonded interactions between monomer units were described by the Morse potential:[11−13]

$$U(r_{ij}) = \epsilon[\exp\{-2\alpha_m(r_{ij} - r_{\min})/\sigma_m\} - 2\psi_{ij}\exp\{-\alpha_m(r_{ij} - r_{\min})/\sigma_m\}] \quad (1)$$

where r_{ij} is the distance between ith and jth monomer units, $\epsilon = 1$ is the energy parameter. At $r_{ij} = \sigma_m$ the potential is equal to zero, while at $r_{ij} = r_{\min} = \sigma_m(1 + \ln(2)/\alpha_m)$ the potential has its minimum equal to $U(r_{\min}) = -\epsilon_{ij}$; the constant $\alpha_m = 24$ determines the shape of potential and how fast it goes to zero. The function ψ_{ij} depends on the type of interacting monomer units and $\psi_{ij} = 1$, if both units are hydrophobic, while $\psi_{ij} = 0$ in the opposite case.

After the coloring procedure is completed, a certain number of cross-links between hydrophobic units is introduced into the system. First, we randomly choose a monomer unit and one of its neighbors that was displaced at a distance smaller than maximum bond length. After linking them, we enabled the system to relax during time that was smaller than relaxation time of the whole system. This step was performed several times until a necessary number of cross-links N_J was introduced into the system. The cross-link was modeled as a regular bond between neighboring monomer units.

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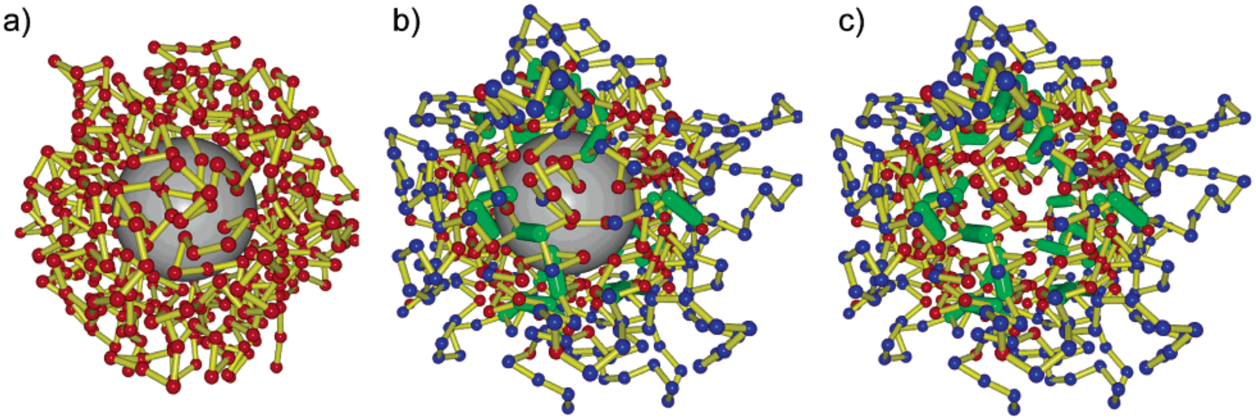

Figure 1. Stages of preparation of copolymer envelope: (a) adsorption of homopolymer chain on a colloidal particle; (b) coloring of the polymer chain (blue color corresponds to hydrophilic and red color to hydrophobic monomer units) and introduction of cross-links (shown as green sticks) to stabilize hollow-spherical structure; (c) elimination of the core particle.

The colloidal particle (p) was modeled as a sphere with diameter σ_p and mass $m_p = \rho_p\sigma_p^3$, where density is $\rho_p = 0.5\sigma_m^{-3}$. To generate the copolymer envelope, we used parental particle of diameter $\sigma_p^o = 5\sigma_m$. The interaction between monomer units and the particle was also described by Morse potential[11-13] with $\epsilon = 1$, $\alpha_p = 12$, and $\bar{r}_{min} = {}^1/_2(\sigma_m + \sigma_p)(1 + \ln(2)/\alpha_p)$. In this case $U(r)$ is essentially zero for $r_{ij} > \bar{r}_{min} + 2\sigma_m$; i.e., the particle interacts with monomer units only in the first and second coordination spheres. Under such conditions, the polymer chain of $N = 512$ monomer units totaly adsorbs at the parental particle; i.e., no free tail is formed.

A simulation was carried out within the framework of the stochastic dynamics by solving Langevin's equations using the LD-velocity Verlet method:[11,12]

$$m_i \frac{d^2\vec{r}_i}{dt^2} = -\frac{\partial U(\vec{r},t)}{\partial \vec{r}_i} - \gamma \frac{d\vec{r}_i}{dt} m_i + \vec{\Gamma}_i(t) \qquad (2)$$

where m_i is the mass and $\vec{r}_i$ is the position vector of ith monomer unit or colloidal particle, $U(\vec{r},t)$ is the interaction potential affecting the monomer unit or the particle at a time t, the friction coefficient $\gamma = 1$, and $\vec{\Gamma}_i(t)$ is a stochastic force satisfying the conditions of Gaussian white noise $\langle\vec{\Gamma}_i(t)\vec{\Gamma}_i(t')\rangle = 2m_i\gamma_i k_B T\delta(t - t')$, where k_B is Boltzmann's constant, T the temperature, and $\delta(...)$ the delta function. Integration was performed with the time step $\Delta t = 0.005\gamma\sigma_m^2/T$.

After the preparation of the copolymer envelope, the particle was eliminated (Figure 1c), and another particle of the diameter ranging from $2\sigma_m$ to $9\sigma_m$ was introduced into the system. A new particle was placed far from the copolymer envelope; i.e., initially it was not interacting with the envelope. During the stochastic motion in the bulk, the particle and envelope came into collision with each other, thus forming a copolymer–particle complex. Each complex was studied during the time $\tau = 2.4 \times 10^4$. Under the thermal agitation the complex was splitting and reassembling again. To evaluate the difference in the interaction of copolymer envelope with particles and thus to distinguish the selectivity properties, we have introduced the following parameter:

$$P\{T,\sigma_p\} = \frac{1}{\tau}\left\langle\int_0^\tau (1 - \delta[E_{EP}(\{T,\sigma_p\},t)])\, dt\right\rangle \qquad (3)$$

where $E_{EP}(\{T,\sigma_p\},t)$ is the energy of interaction between copolymer envelope and particle of size σ_p and the symbols $\langle...\rangle$ denotes an average over an ensemble of 128 independent systems. The function in the integrand expression is equal to unity, when the energy of interaction between copolymer envelope and the particle in not zero, while it is equal to zero for the case, when envelope and particle are separated. Thus, $P\{T,\sigma_p\}$ gives the probability of finding a complex made from the copolymer envelope and a particle of a given size σ_p at the temperature T.

Figure 2 shows the temperature dependence of probability $P\{T,\sigma_p\}$ as a function of particle diameter σ_p for the cases, when copolymer envelope is slightly ($N_J = 16$, Figure 2a) and moderately ($N_J = 48$, Figure 2b) cross-linked. In the first case, we can see that the dependence of $P\{T,\sigma_p\}$ for all the temperatures is monotonically growing with particle diameter σ_p, while in the case of a moderately cross-linked copolymer envelope, we have found a well-pronounced peak for the dependence of $P\{T,\sigma_p\}$ on σ_p. In this case, $N_J = 48$, the preferable particle diameter σ_p^* was found to be about the same as a parental one. However, this result is occasional. In the general case, preferable particle diameter σ_p^* corresponding to the maximum of the plots similar to Figure 2b is not equal to the diameter of parental particle. Results obtained for σ_p^* are summarized in Figure 2c, which gives the preferable particle diameter σ_p^* as a function of the number of cross-links N_J.

Therefore, we can conclude that in the case of moderately cross-linking our procedure allows to obtain a molecular dispenser, i.e., macromolecular object, which can form a selective complex with colloidal particle of a given size. At the same time, the optimum size of a such particle always corresponds to a parental size.

Generally, the structure of the polymer–particle complex can be found from the minimization of free energy that includes the polymer–particle interaction energy, entropies of nonadsorbed monomer units and units localized at the surface of the particle, and, typical for our system, the elastic deformation of cross-linked macromolecule. Such theoretical consideration, following the lines of refs 15 and 16, can explain the growing trend of probability $P\{T,\sigma_p\}$ with particle diameter σ_p and its decrease with temperature T for slightly cross-linked copolymer chain (Figure 2a). Significantly dif-

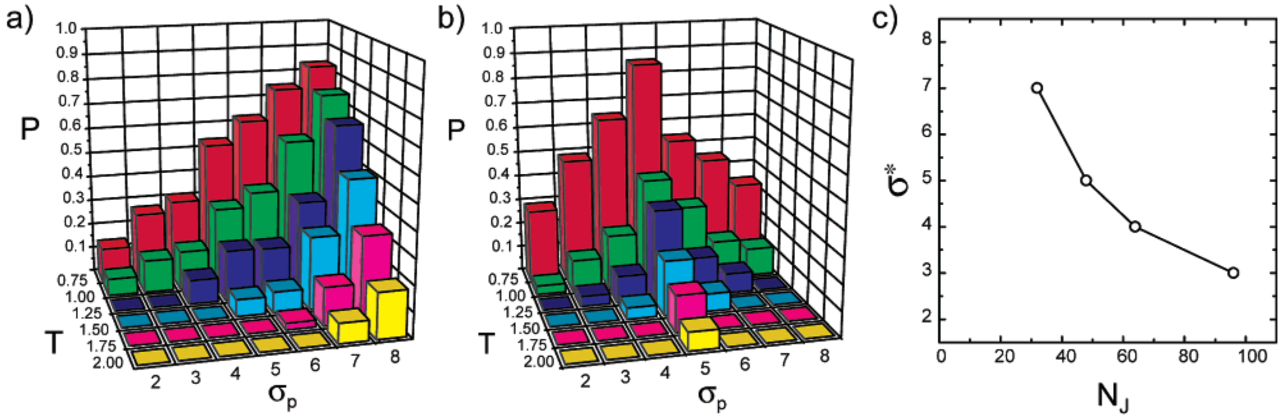

Figure 2. Distribution of $P\{T,\sigma_p\}$ for the case when copolymer envelope has the number of cross-links equal to (a) $N_J = 16$ and (b) $N_J = 48$. (c) Dependence of preferable particle diameter σ^* as a function of the number of cross-links N_J.

ferent behavior for the case of moderately cross-linked copolymer envelope (Figure 2b) is connected with conformational changes in the polymer chain. According to ref 15, when the number of cross-links is small enough, $N_J \ll N^{1/2}$, all junctions contribute mainly to the formation of simple loops along the chain and the polymer molecule as a whole conserves linear structure, while in the case $N_J > N^{1/2}$, the chain becomes really cross-linked, forming a kind of loose network. In our case, when cross-linking was performed in the surface layer of spherical particle, the cross-links stabilized a hollow-spherical structure of the copolymer envelope with meshlike architecture and the cage structure of the central cavity. After elimination of the particle and system relaxation, we have also found a contribution to the stabilization of the hollow-spherical structure through the rearrangement of hydrophilic monomer units between both sides (internal and external) of the copolymer envelope. Thus, the selectivity property of the moderately cross-linked copolymer envelope is based on the existence of a certain mesh size, which restricts the penetration of big particles into the copolymer envelope. Figure 3 demonstrates the mechanism of selectivity of moderately cross-linked copolymer envelope ($N_J > N^{1/2} \simeq 23$) regarding the particle size and shows typical snapshots of complexes formed from the designed copolymer envelope and the particles of different size. One can see that small particle easily penetrates into the copolymer envelope, while the big one is just attached to the side of the envelope. Thus, with increase of the temperature, the complex formed with a small particle $\sigma < \sigma_p^*$ due to smaller interaction energy and big conformational freedom of the envelope can be easily destroyed by the thermal agitation. On the other hand, complexes formed with a big particle $\sigma > \sigma_p^*$ are also not stable because such a particle cannot really penetrate into the envelope and take advantage of being placed in the central cavity. Both these factors explain the peak behavior of probability $P\{T,\sigma_p\}$ with particle diameter σ_p for moderately cross-linked copolymer envelopes.

In conclusion, we suggest the model of molecular dispenser that is selective to the particle size. This model is based on the conformation-dependent design approach for copolymers that also includes additional cross-linking of monomer units. The selectivity property is based on the designed sequence, which is tuned to form the hydrophobic core of the copolymer envelope and to attract the particle, as well as on the existence of cross-links that fix spherical structure of the envelope and restrict penetration of big particles inside it.

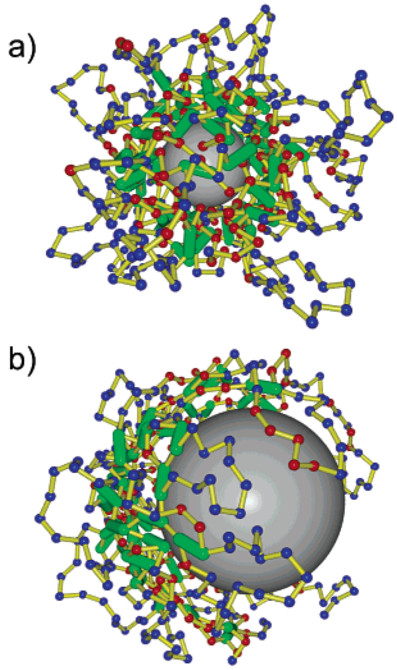

Figure 3. Snapshots of the complexes made from copolymer envelope with $N_J = 64$ and particles of diameter (a) $\sigma = 4$ and (b) $\sigma = 9$.

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surface was achieved by grafting of short poly(ethylene oxide) chains to the thermosensitive poly(isopropylacrylamide) backbone. In particular, it was shown that grafting to a globular surface (a kind of surface "coloring") leads to a more efficient hydrophilization (solution becomes turbid at higher temperatures) than random grafting in the coil conformation (at room temperature). Virtanen, J.; Baron, C.; Tenhu, H. *Macromolecules* **2000**, *33*, 336. Virtanen, J.; Tenhu, H. *Macromolecules* **2000**, *33*, 5970. Virtanen, J.; Lemmetyinen, H.; Tenhu, H. *Polymer* **2001**, *42*, 9487.

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