DOI: 10.1002/masy.201051046

Simulation of Chain Organization in Encapsulated Polymers

*Peter Cifra, Tomas Bleha**

Summary: The dimensional and structural properties of polymers confined into a cavity are computed by the Monte Carlo method as a function of the chain stiffness. The reduction of the size ratio $<R^2>/<R_g^2>$ close to 2, distinctive of compact spheres, is observed at squeezing of chains into a capsule. The plots of the static structure factor $S(q)$ computed for stiff chains show characteristic humps attributed to the toroidal structure. The orientation correlation function is found to be a very sensitive indicator of the globule – toroid transition in encapsulated chains. Evidence is presented that the toroidal morphology is formed in stiff polymers when the capsule radius approaches the chain persistence length ($D \sim P$).

Keywords: computer modeling; Monte Carlo simulation; nanoparticles; persistence length; polymer droplets; shape transition

Introduction

Encapsulation of polymer molecules into micro- and nano-spheres is fundamental to many technological and biological processes.[1,2] Polymer-filled capsules with the porous or hollow structure have found many applications, for example, in coating, printing and biomedical fields. Likewise, in microemulsion systems, the droplets confine the polymer chains inside a spherically closed space. Polymer droplets serve as microcarriers for a broad range of compounds in fluidic devices and drug delivery. Confinement of biopolymers into quasi-spherical spaces is also a ubiquitous phenomenon in nature. A prominent example is the double-stranded DNA packaged inside a bacteriophage capsid. Encapsulation of macromolecules by lipid membranes is used in study of protocellular structures under prebiotic conditions.

As a rule, encapsulated polymers are confined into spaces that are much smaller than their natural size. For example, the dimension of a capsid, between 20 - 120 nm, is comparable to the persistence length of viral DNA (50 nm). Therefore, the encapsulated macromolecules are forced to optimize their properties and chain organization. Despite the considerable progress,[3,4] the theoretical and experimental studies do not yet provide a complete picture of confinement effects in spherical cavities on the micro- and nanoscale. Unresolved issue of the internal organization of confined chains inside a cavity is of the considerable theoretical and practical interest. A notion of a disordered compressed coil (or a globule) is conventionally supposed for synthetic encapsulated polymers. In contrast, in DNA, the ‘‘condensation’’ into the rather compact, ordered toroidal structure was established as a fundamental mechanism enabling the high density packing of DNA inside native confinements.[5]

The aim of the present report is to explore by molecular simulations how the internal structure in a spherical capsule is affected by the chain stiffness. We have computed by the Monte Carlo method the dimensional and structural quantities of polymers of variable persistence length P confined into a sphere. Occurrence of the ‘‘shape transition’’ from the globular to

---

Polymer Institute, Slovak Academy of Sciences, 842 36 Bratislava, Slovakia
E-mail: bleha@savba.sk

Copyright © 2010 WILEY-VCH Verlag GmbH & Co. KGaA, Weinheim

toroidal structure of encapsulated polymers on increase of chain stiffness was observed.

Model and Method

Monte Carlo simulations were based on the coarse-grained worm-like chain (WLC) model. The molecules represented by a sequence of beads connected by springs are confined to a spherical cavity of impenetrable walls of the radius D. The total energy of a chain U is given as a sum of three terms accounting for the variation of bond lengths, nonbonded interactions of beads and the chain bending

$$U = U_r + U_{nb} + U_b \qquad (1)$$

The specification of above terms can be found in Ref.[6,7] The chain stiffness can be modulated by the bending energy penalty $U_b = b(1 + \cos\theta)$, where θ is the chain valence angle and the stiffness parameter $b/kT = P/\sigma$, where P is the persistence length and σ the chain thickness (bead diameter). The persistence length P, expressing the directional memory of bond correlations along the chain, serves as a useful measure of polymer stiffness. The persistence lengths vary,[8] from less than 1 nm for the typical flexible polymers, up to the elevated values for the stiff helical polymers such as poly(hexylisocyanate) (40 nm), DNA (50 nm) and xanthan (120 nm). Three competing length scales were considered in simulations: (a) the chain length up to $N = 2000$; (b) the reduced radius of a confining sphere D/σ that varied from 1 to 150; the radius D comprised an extra term $\sigma/2$ accounting for an accessible volume,[6,7] and (c) the reduced persistence length that varied from $P/\sigma \sim 1$ for the fully flexible chains to around $P/\sigma \sim 35$ for the fairly stiff chains. The chain thickness σ of real polymers differs, for example, it reads about 0.5 nm for poly(ethylene) and 2.5 nm for DNA. To facilitate the comparison of the computed data for chains of different stiffness the typical value of $\sigma = 1$ nm can be chosen.

A variety of dimensional and structural properties of confined chains were calculated, including the mean-square of end-to-end distance $<R^2>$ and the mean radius of gyration $R_g = <R_g^2>^{1/2}$. The chain structure over various length scales can be inferred from the computed single-chain scattering factor $S(q)$

$$S(q) = \frac{1}{N^2}\langle \sum_{i=1}^{N} \sum_{j=1}^{N} \sin(qr_{ij})/qr_{ij} \rangle \qquad (2)$$

where the wavevector $q = 2\pi/x$. Furthermore, the orientation correlation function $<\cos\,\theta(s)>$ of encapsulated chains was evaluated from the averaged scalar product of the all pairs of tangent vectors separated by the arc length s along a chain

$$< \cos\theta(s) > = < \boldsymbol{u}(k)\boldsymbol{u}(k+s) > \qquad (3)$$

Results and Discussion

At first, the results for the mean radius of gyration R_g and the mean-square of end-to-end distance $<R^2>$ are presented. Typical behavior of the relative chain compression with the reciprocal of sphere radius D is shown in Figure 1a for representative cases of flexible and stiff polymers. Qualitatively, squeezing into a capsule proceeds in a similar way for the both types of polymers. Compression increases the volume fraction φ of the polymer inside sphere. At small D the fairly high values of φ of about 0.4 are achieved.

The changes in the chain shape of encapsulated chains can be understand from the plot of the size ratio $<R^2>/<R_g^2>$ in Figure 1b. For both flexible and stiff chains this ratio monotonously decreases on confinement from the value of about 6 normal in a free coil. The size ratio converges at small D to the value of about 2, characteristic of a spherical arrangement. For example, the ratio $<R^2>/<R_g^2> = 2$ was computed[6] for a fully compacted ($\varphi = 1$) ideal random chain in a sphere of radius R_g. Yet, the snapshots of chains simulated in Figure 1 reveal a notable dissimilarity in the internal struc-

Copyright © 2010 WILEY-VCH Verlag GmbH & Co. KGaA, Weinheim

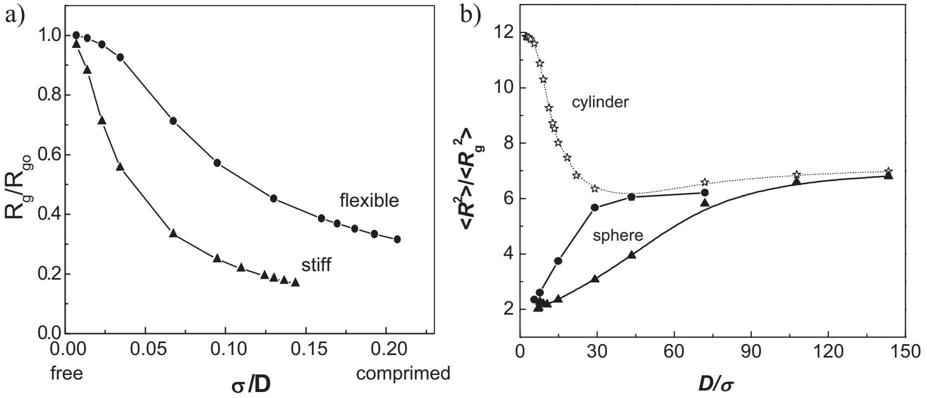

Figure 1.
(a) The change of the radius of gyration R_g (relative to the unconfined chain value R_{go}) on capsule compression for flexible ($P/\sigma \sim 1$, circles) and semiflexible ($P/\sigma \sim 20$, triangles) chains; (b) the related plots of the size ratio $<R^2>/<R_g^2>$ including the data for a chain in a cylinder of radius D/σ ($P/\sigma \sim 20$, stars).

ture between the flexible and stiff encapsulated polymers. The ratio $<R^2>/<R_g^2>$ of global chain dimensions is evidently not able to discriminate between the specific spherical morphologies of encapsulated chains.

Much useful information on the internal structure of encapsulated polymers can be obtained from the plots of the single-chain static structure factor $S(q)$ *vs* q computed according to eq. (2). Fitting the structure factor curves from simulation by the power-law function $S(q) \sim q^{1/\nu}$, where ν is the Flory exponent in the chain size scaling $R \sim N^{\nu}$, gives information on chain organization in different scales of spatial dimensions. In a sphere the computations give qualitative different shape of the function $S(q)$ for the flexible and stiff macromolecules. At small q values and strong confinement, the curves for flexible and stiff chains are similar, exhibiting a slope that is steeper than that for free coils in good solvent (with the exponent -3/5), and approaching that of globule (-3). However, at the smaller length scale, that is, at q around 1 and higher, the structure factors of flexible and stiff chains depart. In this section of the $S(q)$ plot of stiff encapsulated chains a complex shape with a series of maxima is seen in Figure 2a. The maxima in the region of high q are progressively enhanced by reduction of capsule diameter (Figure 2b). On the other hand, the slope of the function $S(q)$ of about -1, found in Figure 2b at high q for a weakly confined stiff chain, is a confirmation of the rod-like character of a chain at this length scale. Hence, since the chain stays locally rigid, the appearance of the maxima on the $S(q)$ function on increasing confinement has to be attributed to the formation of the toroidal structure of stiff chains inside a cavity. The stiff segments become aligned along the internal cavity walls into concentric loops, and depending on the confinement strength a central hole is potentially formed (see snapshots in Figure 2). Additional local correlations should arise between segments in the neighboring loops of a densely packed stiff chain in sphere. The resulting fine structure of $S(q)$ function for this morphology is thus a superposition of the effects of cavity walls and the chain stiffness. Then the first maximum at small q in Figure 2a should correspond to the largest distance of bead pairs, that is, to the average diameter of the toroid. For the stiffness of $P/\sigma = 20$ and the smallest cavity in Figure 2b, of the diameter $2D/\sigma$ of about 15.4, we observe $q_{\max} \sim 0.8$ and thus the diameter of the toroid x is about 8.63. This is still for a fairly homogeneous structure, without a pronounced hole in the middle of structure,

Copyright © 2010 WILEY-VCH Verlag GmbH & Co. KGaA, Weinheim

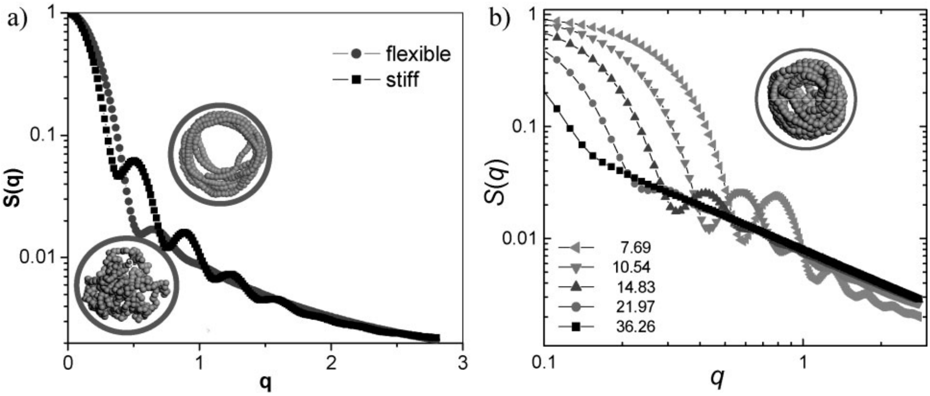

Figure 2.
(a) Plots of the single-chain structure factor $S(q)$ for flexible ($P/\sigma = 1$) and stiff ($P/\sigma = 35$) polymers of $N = 400$ confined in a sphere of $D = 10.54$; (b) The related plots for chains of $P/\sigma = 20$ in a cavity of the size D/σ indicated in the legend.

and thus the computed diameter x is smaller than the cavity diameter. For the typical toroidal structure of the stiff chain of $P/\sigma = 35$ and $2D/\sigma = 21.08$ the maximum lies at $q_{\max} \sim 0.5$ in Figure 2a and the toroid diameter x is about 13.3.

Finally, we address the directional correlations of the tangent vectors in encapsulated chains computed according to eq. (3). The correlation function $<\cos \theta(s)>$, readily measured in experiments, is frequently employed in determination of the persistence length of polymers. The simulation reveals a striking sensitivity of the correlation function of encapsulated polymers to the chain morphology inside capsule. For flexible chains the function $<\cos \theta(s)>$ exhibits an exponential decay of the bond correlations along the chain arc (Figure 3a), similar to that established in unconfined polymers. On the other hand, in stiff chains, the function $<\cos \theta(s)>$ shows a periodic character. The negative values of $<\cos \theta(s)>$ seen in oscillations are clearly associated with an opposite orientation of tangent vectors in a looped chain. In this way, the oscillatory behavior of $<\cos \theta(s)>$ serves as an unequivocal identification of the toroidal structure of an encapsulated polymer. It is seen that periodicity of oscillations becomes more pronounced in smaller cavities (Figure 3b).

The occurrence of toroidal chain morphology and of associated oscillations of the function $<\cos \theta(s)>$ in stiff polymers evidently depends on the strength of imposed confinement. For example, Figure 3b suggests that the oscillatory behavior develops when the reduced capsule radius D/σ drops well below 36. Elucidation of the conditions controlling a cross-over from the disordered to the toroidal structure in stiff polymers is worthy of attention. A sketch in Figure 4 illustrates that the onset of oscillations in the function $<\cos \theta(s)>$ is related to the natural radius of curvature R of a chain and its interplay with D. The worm-like chain model provides the relation of the natural radius R to the persistence length. The persistence length P can be determined from the decay of orientation correlations along the chain, $<\cos \theta(s)> = \exp(-s/P)$. The change of the chain direction angle within one persistence length ($s = P$) is 1.19 rad and this also defines the average local radius of curvature R of the chain, $1.19 = P/R$.

The following qualitative reasoning is presented in Figure 4 using the relation $R = 0.84P$. When the radius of cavity D is much larger than the natural radius of curvature (or the persistence length), the chain is unhindered and adopts the random disordered conformation (upper panel).

Copyright © 2010 WILEY-VCH Verlag GmbH & Co. KGaA, Weinheim

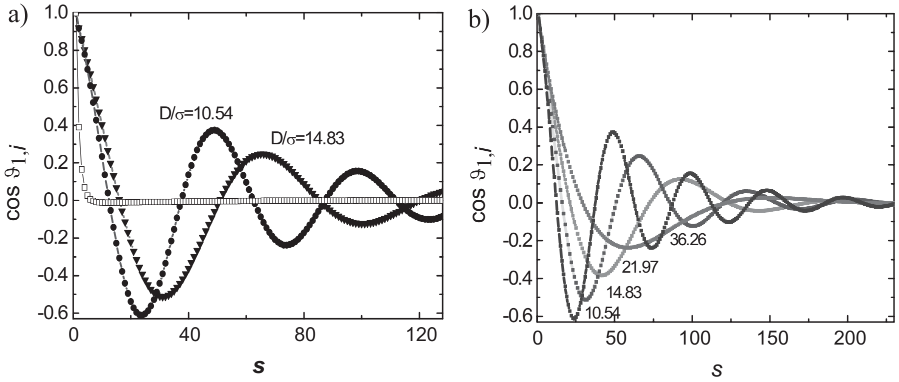

Figure 3.
(a) Plot of the orientation correlation function from eq. (3) for flexible ($P/\sigma = 1$) polymers of $N = 400$ confined in a sphere of $D/\sigma = 10.54$ The same for the stiff ($P/\sigma = 20$) polymers and $D/\sigma = 10.54$ and 14.83; (b) The related plots for chains of $P/\sigma = 20$ in a cavity of the size D/σ indicated.

However, when the cavity radius falls close to the persistence length, a stiff chain favors an alignment along the internal cavity walls, rather than the bending in excess of that allowed by the chain persistence.

At the critical condition $D \approx R \approx P$, a shape transition of a disordered compact coil (globule) into the spool-like structure should take place in a capsule. In other words, for the encapsulated semiflexible polymer of stiffness $P = 40\,\text{nm}$, such as poly(hexylisocyanate), the toroidal structures should arise in cavities of the radius smaller than 40 nm. Remarkably, simulations suggest that development of the toroidal structure discovered in DNA is not a outcome of some specific interactions exclusive for DNA, but it is a general consequence of minimization of the bending penalty of stiff polymers on confinement in a sphere.

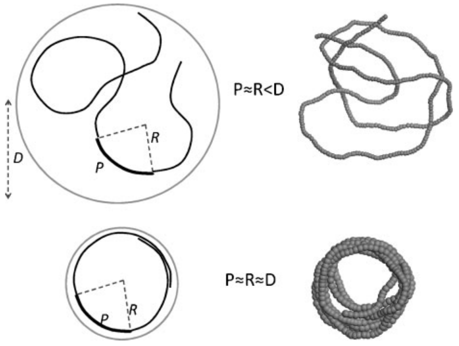

Figure 4.
Sketch of the crossover condition for the globule-toroid shape transition of an encapsulated stiff chain and the respective snapshots of chains for $N = 400$, $P/\sigma = 35$ and the cavity sizes $D/\sigma = 28.57$ and 10.54.

Recapitulation of the simplified picture ensuing from simulations is as follows. When flexible polymers of the persistence length around 1 nm are encapsulated, the disordered structure with no loops arises, regardless of the capsule radius. In stiff polymers of the natural origin (such as DNA, xantan), or in the synthetic helical or biomimetic polymers, the toroidal morphology inside a cavity is preferred over the disordered one when the capsule radius becomes smaller than the polymer persistence length. The nature of the shape transition needs yet to be explored in a detail. Nevertheless, there are indications of the more general phenomenon since the criterion $D \sim P$ seems operating also in other types of confinement, such as in disappearance of the hairpin structures of stiff biomacromolecules in channels.

Acknowledgements: This work was supported by the Science and Technology Assistance Agency under the contracts No. APVV-0079-07 and No. APVV-0607-07, and by VEGA grants 2/6116/26 and 2/6014/26. This work also benefited from the Centers of Excellence Program of the Slovak Academy of Sciences (COMCHEM).

[1] X. D. Feng, Z. X. Jin, *Macromolecules* **2009**, *42*, 569.
[2] M. D. Barnes, A. Mehta, P. Kumar, G. B. Sumpter, D. W. Noid, *J. Polym. Sci. Polym Phys.* **2005**, *43*, 1571.
[3] D. Nykypanchuk, H. H. Strey, D. A. Hoagland, *Macromolecules*, **2005**, *38*, 145.
[4] P. Cifra, *J. Chem. Phys.* **2006**, *124*, 024706.
[5] A. S. Petrov, S. C. Harvey, *Structure*, **2007**, *15*, 21.
[6] P. Cifra, Z. Benkova, T. Bleha, *J. Phys. Chem. B*, **2008**, *112*, 1367.
[7] P. Cifra, Z. Benkova, T. Bleha, *Faraday Discussions* **2008**, *139*, 377.
[8] T. Norisuye, *Prog. Polym. Sci.* **1993**, *18*, 543.

Copyright © 2010 WILEY-VCH Verlag GmbH & Co. KGaA, Weinheim