Field-Induced Deformation and Structure Changes in a Magnetic Polymersome: Many-Particle Simulation

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Abstract. Coarse-grained molecular dynamics simulation is performed to analyse structure and deformation response of a magnetic polymersome – a submicron hollow capsule whose membrane is made of amphiphilic block-copolymer, and the intramembrane space is filled with magnetic nanoparticles. The major prospects of these objects are related to controlled drug release. The developed many-particle model is used to calculate equilibrium magnetized configurations of polymersomes with different intensity of magnetic interparticle coupling. The analysis of those data reveals that under external magnetic field, an initially spherical capsule stretches along the field direction assuming a spheroid-like shape. This behaviour is caused by the field-driven tendency of the nanoparticles to aggregate inside the polymersome membrane. At weak interparticle magnetic interaction no extended chains are observed. Accordingly, the deformation and density redistribution are relatively small. In a polymersome with strong interparticle coupling the nanoparticles self-organize in long chains aligned with the field, and this induces considerable elongation of the polymersome along with accumulation of the majority of the nanoparticles in the “equatorial” zone of the membrane of the capsule.

1. Introduction
The promising prospects of actively developing nanomedicine and theranostics are connected with synthesis of remotely-controlled polymeric microcarriers for drugs. Embedding of magnetic nanoparticles (MNPs) in submicron-size entities open vast opportunities of induced transport and drug release. A particular type of such microcontainers are magnetic microgels (microferrogels) [1, 2] comprising several hundred MNPs grafted to or trapped in a hydrogel molecular mesh. External magnetic fields enhance the interparticle magnetic coupling and make the MNPs to move both translationally and orientationally. The particles, experiencing resistance on the mesh, transfer some part of their motion to the network, thus, making a microferrogel sample to deform (shrink or swell) and to change its structure.

A fascinating example of remotely-driven containers is magnetic polymersomes (MPSs) [3]. These objects are hollow submicron capsules whose membranes consist of two layers of amphiphilic block-copolymer molecules with hydrophobic groups of each layer looking inward. The intramembrane space of an MPS has enough room to accommodate a monolayer of MNPs [4]. Figuratively speaking, the MPS membrane contains a small sample of a 2D ferrofluid. In the absence of external magnetic field, the intramembrane MNPs are either in a “gaseous” state or form chain-like structures due to their magnetic dipole-dipole interaction. However, independently of the particle aggregation, the pressure distribution in the membrane is isotropic on the average. Such an MPS, when suspended in a fluid, minimizes its surface energy and assumes spherical shape maybe to within some fluctuations.

An applied field aligns the MNP magnetic moments, this straightens the particle chains and makes the intramembrane pressure distribution non-uniform. Responding to those changes, the membrane deforms, and the MPS assumes anisometric shape. Elongation in the direction of the field was detected.
in experiments for synthesized MPSs [5] as well as in observations of model micron-sized colloidosomes [6].

The field-induced deformation is accompanied by the change of the volume of the internal cavity of the MPS, so that, depending on the particle and membrane properties, the polymersome might either release its content (e.g., a drug solution) or to suck in the fluid it is suspended in.

Along with this direct field-driven release/uptake mechanism, the field might have an implicit effect on the mass transfer of the carried chemical through the MPS wall. Namely, the filed-induced redistribution of MNPs inside the membrane modulates local permeability of the latter and, due to that, might quite strongly impede the diffusion transport through the wall. This issue, formerly, never addressed in theoretical literature, is the main goal of the present paper. In below we show that in an MPS elongated in the field direction, the “polar” zones are virtually free of the MPSs whereas the “equatorial belt” is enriched in them.

The description that we use here is based on the coarse-grained approach of many-particle dynamics. It had been successfully applied for simulation of magnetic gels [7–9]. One of the main its advantages is that it binds explicitly the degrees of freedom of all the elements of the system: both the polymer molecules and MNPs. In below, before presenting our particular results, we briefly outline the coarse-grained molecular model that we use; a more detailed account on that technique could be found in [10].

The geometry of the model is shown in figure 1. Two concentric shells form the membrane walls. The monolayer of magnetic beads with built-in magnetic moments is placed inside the membrane. As the interactions between the particles belonging to either shell are purely elastic, the initial equilibrium shape of the MPS is spherical. Note that the constructed MPS possess also some amount of intershell elastic bonds that helps to keep the membrane thickness approximately constant. The polymer shells are impenetrable for MNPs. As to the MNPs themselves, they are taken to be spheres of identical size bearing identical magnetic moments of constant magnitude. The particles are magnetically isotropic and interact with each other by way of dipole-dipole potential.

The equilibrium configuration, i.e., positions of all the particles (beads) under any set of given conditions (the level of MNPs interaction, magnitude of the external field, etc.), is calculated from Newton equations of motion for each i-th bead:

$$m_i \ddot{r}_i = F_i^\text{shell} - \zeta \dot{r}_i + f_i(t),$$

where $m_i$ is the bead mass; the two last terms in the right-hand side are: the translational friction force with coefficient $\zeta$ and the random force produced by Langevin thermostat [11], respectively. The force $F_i$ is derived from interaction of i-th particle with other elements and is denoted as $F_i^\text{shell}$ for the shell beads and as $F_i^\text{MNP}$ for the MNPs, see [10] for details.

Computer simulations of the polymersome deformation in external field were performed in software ESPResSo [12]. The major parameters which define the magnetodeformation effect are:

- ratio of the pairwise dipolar magnetic interaction energy of particles of diameter $d_{\text{MNP}}$ and magnetic moments $\mu$ to thermal energy: $\lambda = \mu^2 (d_{\text{MNP}} k_B T)^{-1}$;
- ratio of the energy of interaction of magnetic moment $\mu$ with external field of strength $H_0$ to thermal one: $\xi = \mu H_0 (k_B T)^{-1}$.

2. Results and Discussion

The above-described coarse-grained model was applied to investigate structural changes which cause the deformation of an MPS in a uniform external magnetic field. The membrane of the polymersome contains a fixed number of MNPs. In the presented here simulation template it equals 393 that is comparable to that in actually synthesized samples [13]. In the geometry scale of the model, the nanoparticle volume fraction in the intramembrane space is about $\varphi_{vol} = 11\%$.

Two types of model polymersomes were studied. The MPS of the first type are filled with MNPs characterized by weak interparticle magnetic coupling: their dipole-dipole interaction parameter is $\lambda = 1$. The MPS of the second type contains the MNPs which interact much stronger, for them $\lambda = 5$. In the performed computer simulations, the objects of both types were exposed to gradually increasing magnetic field: parameter $\xi$ grew from 0 to 10.

Under these conditions, the randomly oriented magnetic moments of MNPs are stimulated to align with the direction of the applied field. Notably, the weakly interacting MNPs do not display a pronounced tendency for aggregation. To the contrary, the strongly interacting MNPs readily form elongated columns (chains) parallel to the field direction. This difference in structuring clearly manifests itself if to compare the extent of elongation of the MPS of both types.

To assess the MPS deformation, we define the aspect ratio of an anisometric object as

$$R = 2h/(a + c),$$

where the dimension parameters are presented in figure 2 as follows from equation (2), $R > 1$ for a prolate spheroid and $R < 1$ for an oblate one. In simulations, the aspect ratio is calculated by evaluating the diametrically opposed extreme points in three perpendicular directions.

![Figure 2. Scheme of finding of deformed polymersome axes to define aspect ratio as it is specified in equation (2).](image)

The obtained dependences of the MPS aspect ratio on the nondimensional strength $\xi$ of applied field are plotted in figure 3(a) for $\lambda = 1$ and in figure 3(b) for $\lambda = 5$. The numerical data (dots) were approximated by sigmoid curves (red lines). For weak dipolar interactions the energy of thermal fluctuations is comparable with the energy of MNPs magnetic attraction, and, therefore, the extent of aggregation is rather low. As figure 3(a) shows, up to $\xi \approx 3$ the data most probably just fluctuates. Out of this region, i.e., at higher fields, the fluctuations fade out, however, so that one may infer that the attained aspect ratio is indeed different from unity. Nevertheless, it always remains quite small and saturates at the level of about 5% above $R = 1$.

For the particles with pronounced tendency for field-induced aggregation ($\lambda = 5$), the effect is several times greater. The fluctuation region occupies a more narrow interval (up to $\xi \approx 2$); whereas beyond this range the aspect ratio grows as high as 17% at $\xi \approx 10$ and does not seem completely saturated.
Figure 3. Aspect ratio dependences on the strength of the applied field $\xi$ for model polymersomes with intramembrane content of MNP filler $\varphi_{\text{cd}} = 11\%$; pane (a) – weakly interacting MNPs ($\lambda = 1$); pane (b) – strongly interacted MNPs ($\lambda = 5$). Dots resemble the data obtained in numeric experiments, red lines are sigmoid curves used as eye guides.

The shape changing process in the MPS with $\lambda = 5$ is accompanied by rearrangement of the MNPs chains. Under the action of the field, previously existing randomly oriented chains straighten and strive to settle along the field direction. Being confined within a quasi-spherical membrane, they have to bend assuming the curved contours resembling the Earth meridians. Those arrangements are never perfect, however, due to the thermal motion of the MNPs constituting the chains.

As the chains are magnetized in the same direction, they repel each other and strive to find the positions which are most remote from each other. Therefore, the azimuthal distribution of the particles (we take the direction of the field as the polar axis) becomes angular-modulated. This effect is easy to foresee, and the spatial scale of this type of the MNP density non-uniformities caused by it is small in comparison with the overall size of the MPS. Indeed, those perturbations is of the same order of magnitude as they are in a non-magnetized MPS where the chains are oriented at random.

The distribution of MNPs in a magnetized polymersome with respect to polar angle is a more complicated problem. If to consider it from the magnetostatic viewpoint, one encounters two opposing tendencies. On the one hand, any chain reduces its energy the more the longer it is. Thus, the most favorable pattern for a single chain is to stretch along “meridian” from pole to pole. On the other hand, the mutual repulsion enhances the closer are the neighboring chains, and this means that the chains would avoid the places where their parts come too close to one another. In the given confined geometry those places are located in the poles of the MPS. Therefore, to within the inaccuracy caused by Brownian motion, one would, in general, expect that the “polar” zones are depleted of the MNPs.

To get quantitative notion of the MNPs distribution between the polar and equatorial zones of the considered MPS, we do the following. Two boundary meshed surfaces of a simulated magnetized MPS are replaced by the corresponding spheroids whose semi-axes are taken from evaluation of the aspect ratio.

We denote the major and minor axes of the inner spheroid as $L_{\text{in}}$ and $l_{\text{in}}$, respectively, and for the outer one as $L_{\text{out}}$ and $l_{\text{out}}$, see figure 4. With allowance for the symmetry of the MPS body, it suffices to consider only half of the object. The residual hemisphere is crossed by a stack of planes perpendicular to the direction of external field. The lines where these planes intersect the inner and outer spheroid surfaces make respective “parallels” if to stick to the above-adopted geographical terminology.

Any pair of neighboring planes cut out of the space between the nested half-spheroids a circular ring of specified thickness and height (measured along the polar direction). Then the number of MNPs in a given ring is counted and divided by the volume of the ring. Taking the volumes of the inner and outer half-spheroids as
the resulting number density is presented in the form

$$n = \frac{N_{x_1,x_2}}{V_{out} - V_{in}},$$  \hspace{1cm} (4)$$

where $N_{x_1,x_2}$ is the number of the MNPs located in the ring bounded by the planes crossing the longer semi-axis in the points with coordinates $x_1$ and $x_2$, see figure 4.

Concentration distributions $n$ of MNPs as functions of the polar angle $\theta$ for the polymersomes with weak and strong magnetic dipolar interaction are presented in figures 5 and 6 for several values of nondimensional external field $\xi$. As well in those figures are shown the snapshots of top view for each configuration.
Figure 5. An MPS with volume content of the nanoparticles $\varphi_{\text{vol}} = 11\%$ and dipolar parameter $\lambda = 1$; snapshots of top views in the field directed perpendicularly to the plane of view) and polar angle dependences of the MNP concentration distribution (scaled in inverse MNP volume $V_{\text{MNP}}^{-1}$) for the field strength $\xi = 0$ (a), 2 (b), 4 (c), 6 (d), 8 (e), 10 (f).
Before commenting figures 5 and 6 we would like to make an important remark. One should consider the data presented in the plots as reliable only approximately up to $\theta \approx 60^\circ$. Above that angle (in the near-polar zone), the slicing procedure that we use does not work well: the volume of the sliced rings becomes comparable with that of an MNP, and calculation errors (numeric fluctuations) become huge. To get notion of the particle distribution in the near-polar zone it is better to consult the snapshots: although qualitatively, but they are more correct for that case.
The snapshots of figures 5 and 6 illustrate how, under enhancement of the field, the MNP concentration in polar zones of an MPS gradually changes from notably dense pattern, as in figure 5(a), to more rarefied distribution, as in figure 5(f). This tendency is rather weak at $\lambda = 1$ and very well pronounced at $\lambda = 5$. As the angle plots show, the concentration distribution at zero field is uniform for any $\lambda$.

In real MPSs, uneven concentration distribution may strongly affect to permeability of membrane for low molecular weight content. Namely, acting on the capsule by external field it is possible to change structural organization of magnetoactive particles and thereby cause deformation and control the release of substance. For the model MPSs with intensively interacted MNPs (figure 6) decreasing character of concentration expressed even stronger. At zero field, see figure 6(a), the MNPs are organized in randomly oriented chains encircling MPS membrane, that is why the large-scale initial distribution is uniform. With enhancement of the field strength, the aggregates rebuilt in the chains stretched along meridional direction (simultaneously, the aspect ratio changes significantly). In this case the poles are indeed strongly depleted of the MNPs, see the corresponding snapshots.

3. Conclusions
The developed coarse-grained model of a magnetic polymersome was applied to study the field-induced deformation and internal restructuring. The advantage of the employed many-particle approach is that it allows one to estimate (and partially quantify) the mechanical and structural changes in a magnetopolymer capsule. Visualization of the equilibrium nanoparticles configurations makes it possible to observe and confirm the redistribution of nanoparticles in the intramembrane space. The main conclusion is that the effect of nanoparticle accumulation in the equatorial zone is found, and the dependence of the effect on the intensity of intraparticle magnetic interaction is revealed.

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