Hard-colloidal particles in contact with fluctuating membranes

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A model to study the structural and thermodynamic properties of hard-colloidal particles in contact with fluctuating membranes by means of Monte Carlo simulation is proposed. To test the accuracy of our model, we compare the density profile of a system composed of non-interacting point-like particles with the analytical expression derived by Bickel *et al.* [*Phys. Rev. E* **70** (2004) 051404]. This model is applicable to colloids with finite size and it can easily be extended to binary systems or systems with long-range (Coulomb-like) interactions.

Keywords: Colloids; membranes; Monte Carlo simulation.

Se propone un modelo que utiliza simulación de Monte Carlo para estudiar las propiedades estructurales y termodinámicas de esferas duras coloidales en contacto con membranas fluctuantes. Para verificar la precisión de nuestro modelo, comparamos el perfil de densidad de un sistema compuesto por partículas puntuales no interactuantes con la expresión analítica derivada por Bickel *et al.* [*Phys. Rev. E* **70** (2004) 051404]. Este modelo es aplicable al caso de coloides con tamaño finito y puede ser fácilmente extendido a sistemas binarios o sistemas con interacciones de largo alcance (tipo Coulomb).

Descriptores: Coloides; membranas; simulación de Monte Carlo.

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1. Introduction

Biological membranes are made of three major components: lipids, proteins and sugars. All membranes have a common general structure: two-layered sheets of lipid molecules. Proteins are embedded in them. The lipid and protein molecules are held together mainly by non-covalent interactions whereas sugars are attached by covalent bonds to some of the lipid and protein molecules. They are found on one side of the membrane only, for example, on the outer surface of the plasma membrane [1]. There are three major types of lipids found in biological membranes: phospholipids, glycolipids and cholesterol. They each play different roles in the membrane (see for example, Ref. 2 and references therein).

Many biological processes are controlled by the interactions of macromolecules with the cell membrane. Besides highly specific interactions of a steric and chemical nature, there are also entropic force fields which are omnipresent but whose actions depend only on geometrical features. These entropy-driven forces are commonly known as *depletion forces* and can be exploited to organize self-assembled structures [3, 4].

A generic feature of membranes is, however, that they are not flat. The variation of the local curvature leads to a new quality of the depletion forces in that they are no longer directed only normal to the surface, as in the case of flat wall or a wall with a constant curvature, but there is also a lateral component which promotes transport along the membrane. So far there are no systematic theoretical studies available which accurately predict this important curvature dependence of the depletion forces. The theoretical description of this phenomenon requires advanced techniques which must be adapted to the study of depletion potentials close to arbitrarily shaped substrates. Therefore, in this work we introduce a model for studying hard-colloidal particles in contact with fluctuating membranes by means of Monte Carlo computer simulations. This model makes it possible to include both the elastic properties of the membrane and the finite size of the colloids; elements which are crucial to the development of a more complete description of the depletion forces in a membrane-colloid system. Also, our model has an exceptional advantage: it can easily be extended to binary systems or systems with long-range (Coulomb-like) interactions.

After the present introduction, the next section is dedicated to a description of the membrane model, where the Helfrich Hamiltonian is introduced [5]. In Sec. 3, we describe in detail how it is possible to transform the mathematical model in a discrete version which is useful in carrying out a membrane-colloid simulation. In Sec. 4, we apply our model to studying the density profile of point-like particles close to the membrane. We also test our results with analytical calculations [6]. Finally, the paper ends with a section of conclusions.

2. Membrane model

Clearly, biological membranes are very complex objects. To understand certain aspects of the behavior of cell membranes, it is advantageous to study simpler objects composed solely of lipids. Two systems composed of a pure phospholipid bilayer are vesicles and planar bilayers. Vesicles are "bags" up to 100 μm in diameter consisting of a phospholipid bilayer that encloses a central aqueous compartment [7, 8]. They are formed by mechanically dispersing phospholipids in water. Planar bilayers are formed across a hole in a partition

that separates two aqueous solutions [7, 8]. Below, we shall confine ourselves to a discussion of the properties of membranes composed of lipids and neglect the complexity arising through enclosed proteins, the glygocalyx and the cytoskeleton present in cell membranes.

Lipid bilayers combine exceptional elastic properties which would be difficult to obtain with technical materials. The bending modulus is smaller than those of a 5 nm thick shell made of polyethylene, by a factor of 1000, and the shear modulus by a factor of 10,000, but the area compression modulus is almost as large as those of the polyethylene shell, which makes the bilayer virtually incompressible [7]. The bending rigidity of lipid bilayers is between 5 and 100 $k_B T$ (k_B is the Boltzmann constant and T the temperature) at room temperature. Due to the low bending rigidity, membranes undergo thermal shape fluctuations, which can be visualized by interference contrast microscopy [9].

Keeping in mind the properties mentioned above, Helfrich proposed a Hamiltonian which describes a fluctuating membrane [5]. In this approximation, a membrane is seen as a three-dimensional fluctuating surface, S. Monge parametrisation is commonly used to describe the membrane position in terms of height $h(x, y)$ above the underlying reference plane as a function of the orthonormal coordinates x and y (see Fig. 1).

There are two contributions to the energy of the membrane: surface tension and curvature energy [10]. Therefore, it is possible to express the total energy (or Hamiltonian) of the system in the following form [6]

$$H_m(h) = \frac{1}{2} \int \left[\kappa \left(\nabla^2 h \right)^2 + \gamma \left(\nabla h \right)^2 + \mu h^2 \right] dx dy, \quad (1)$$

where κ, γ and μ are the bending, surface tension and membrane mass, respectively.
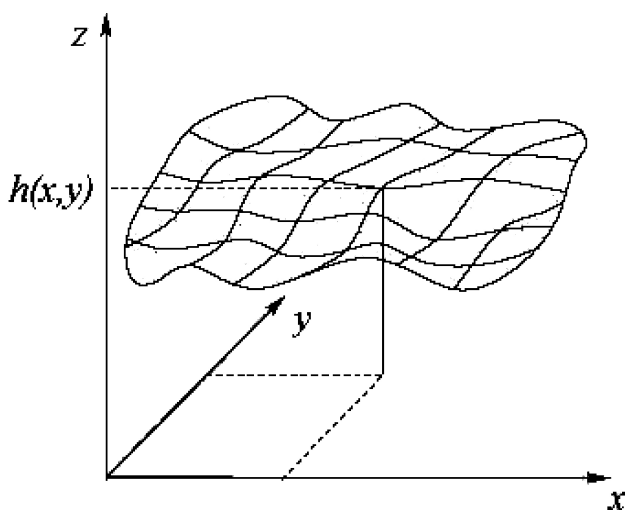

FIGURE 1. Sketch of the Monge parametrisation. Each point of this three-dimensional surface is described by the coordinates $(x, y, h(x, y))$.

The height-height correlation function is defined as

$$G \left(\mathbf{r} - \mathbf{r}' \right) = \langle h \left(\mathbf{r} \right) h \left(\mathbf{r}' \right) \rangle_0 - \langle h \left(\mathbf{r} \right) \rangle_0 \langle h \left(\mathbf{r}' \right) \rangle_0 \quad (2)$$

$$= \int \frac{d\mathbf{q}}{(2\pi)^2} \frac{e^{i\mathbf{q} \cdot \mathbf{r}}}{\hat{\kappa} q^4 + \hat{\gamma} q^2 + \hat{\mu}}, \quad (3)$$

where $\hat{\kappa} \equiv \beta \kappa$, $\hat{\gamma} \equiv \beta \gamma$ and $\hat{\mu} \equiv \beta \mu$, being $\beta = (k_B T)^{-1}$, $\mathbf{r} = (x, y)$ is the transverse vector, and the thermal averages $\langle \cdots \rangle_0$ are performed with the Helfrich Hamiltonian (1) in the absence of particles. For a bilayer without surface tension ($\gamma = 0$), the integral over the Fourier modes leads to

$$G \left(\mathbf{r} \right) = -\frac{4}{\pi} \xi_\perp^2 \, kei \left(\sqrt{2} \frac{\mathbf{r}}{\xi_\parallel} \right), \quad (4)$$

where $kei(x) = \text{Im}[K_0(x e^{i\pi/4})]$ is a Kelvin function [6]. We then define the mean roughness of the membrane $\xi_\perp = G(\mathbf{0})^{1/2} = 2^{-3/2} \left(\hat{\kappa} \hat{\mu} \right)^{-1/4}$, and the in-plane correlation length $\xi_\parallel = 2^{1/2} \left(\hat{\kappa} / \hat{\mu} \right)^{1/4}$ characterizing the exponential decay of $G(\mathbf{r})$ at large distances

$$G \left(\mathbf{r} \right) \sim e^{-r/\xi_\parallel}, \quad r \gg \xi_\parallel. \quad (5)$$

Figure 2a shows the behavior of the correlation lengths, $\xi_\perp$ and $\xi_\parallel$, when the bending κ changes keeping the value of μ constant. In the limiting case where $\kappa \to 0$ (where thermal fluctuations easily modify the shape of the membrane), also $\xi_\parallel \to 0$, but if $\kappa \to \infty$ (flat wall) then $\xi_\parallel \to \infty$; and $\xi_\perp$ behaves inversely at both limits. Figure 2b shows the variation in both correlation lengths for a constant κ by changing the membrane mass. The behavior is very similar in both correlations, *i.e.* they decay in an exponential-like fashion and both go to zero when $\mu \to \infty$. On the other hand, $\xi_\perp$ and $\xi_\parallel$ make it possible to scale all the observable quantities.

3. Simulation of the membrane-colloid system

3.1. Lattice model

A membrane is discretized as a two-dimensional $N_L \times N_L$ square lattice with lattice constant a (see Fig. 3). A given number of lattices N_L defines the lateral length of the membrane, $L = a N_L$, and the projected area of the membrane is $A = a^2 N_L^2$. All lengths in the system could be scaled with the lattice constant. Surface is given by means of the position vector $\mathbf{S} = \mathbf{S}(\mathbf{r}, h(\mathbf{r}))$, where ($\mathbf{r} \in A$) is the vector on the xy-plane and h is the field in the z-direction. In our simulations, the h-field represents the thermal fluctuations. From the simulation point of view, it is only a random number ranging within the interval $[-h_{max}/2, +h_{max}/2]$, where h_{max} is a parameter which is controlled according to the ratio between the accepted and total Monte Carlo steps of the membrane.
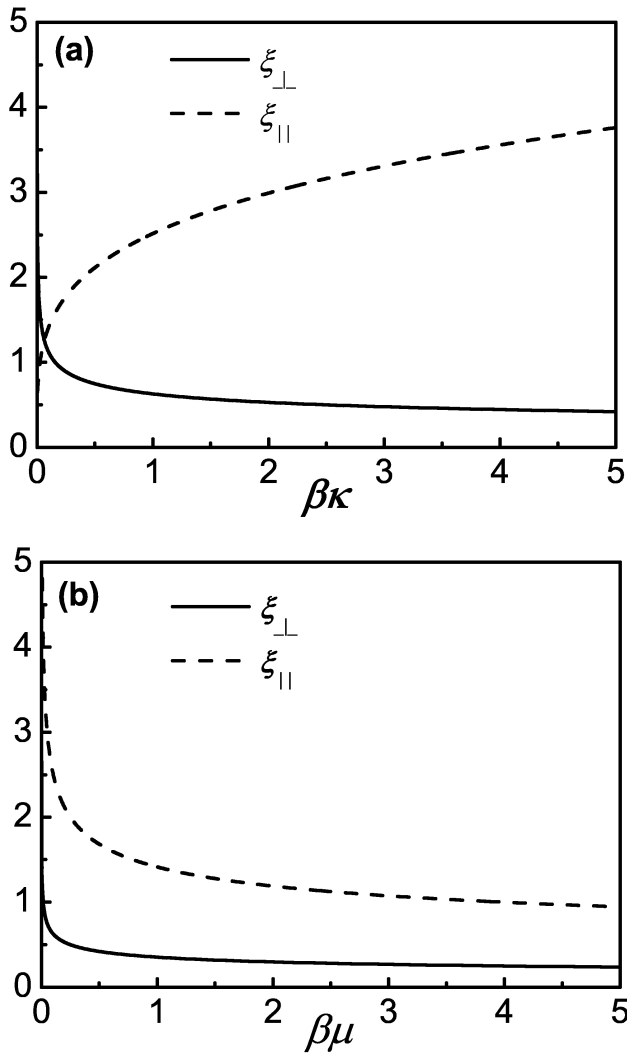
FIGURE 2. a) Correlation length as a function of the rigidity of the membrane κ for a given value of μ. b) Correlation length as a function of the mass of the membrane μ, for a given value of κ.
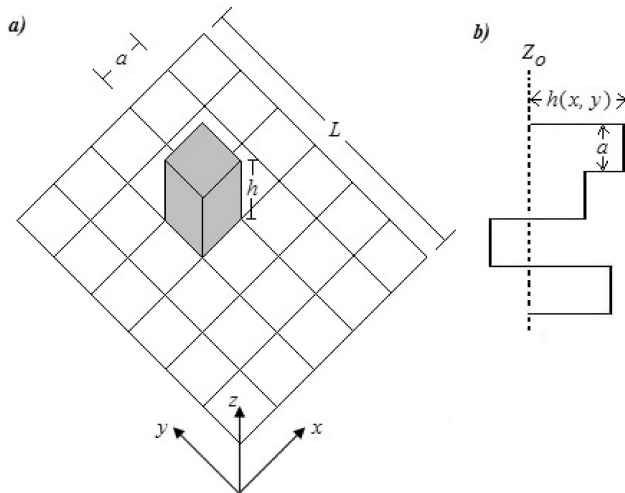

FIGURE 3. Simulation model. a) Top view and b) side view of the discrete representation of the membrane. Surface is given by the position vector $\mathbf{S}\,(x, y, h\,(x, y))$, where the height of the lattice site ij is given by the field h_{ij}.

We summarize here the main steps for simulating the membrane:

1. The membrane starts in an initial configuration, and there are two choices:

   (a) Every membrane site is set as $h_{ij} = 0$ (flat wall).

   (b) A random configuration, where all sites of the membrane are set in a random position.

2. The energy of the initial configuration, E_i, is calculated with the Helfrich Hamiltonian (1).

3. Every membrane site is moved a distance $h_{ij} = h_{max}(\text{rand}() - 0.5)$, where rand() is a random number defined in the interval [0, 1].

4. The energy of the new configuration, E_n, is calculated again through Eq. (1).

5. The Metropolis criterion [11] is applied to decide if the new configuration is accepted or rejected.

6. Update all quantities.

7. Return to step number three.

Before calculating statistical averages, it is necessary to guarantee that the system has reached thermal equilibrium. To reach thermal equilibrium, one can verify the energy of the system. If the energy fluctuations around the mean energy value, $\bar{E}$, are much smaller than $\bar{E}$, then the system is in thermal equilibrium.

The energy must be calculated using the Helfrich Hamiltonian; the discrete gradient and Laplacian operators are given by [12]:

$$\nabla^2 h_{ij}\,(x, y) = h_{i+1j} + h_{i-1j} + h_{ij+1} + h_{ij-1} - 4h_{ij},$$

$$[\nabla h_{ij}\,(x, y)]^2 = (h_{i+1j} - h_{ij})^2 + (h_{ij+1} - h_{ij})^2. \tag{6}$$

The approximation of these discrete operators depends on the size of the lattice constant a. A good approximation is to have a high number of lattices, but requiere more CPU time.

The quantity h_{max} corresponds to the maximum Monte Carlo step. For an efficient sampling, it is essential that h_{max} be neither too large (most of the suggested configurations will be rejected) nor too small (almost all of the suggested configurations are accepted). A convenient measure for efficiency is the acceptance ratio defined by

$$a_r \equiv \frac{\text{number accepted steps}}{\text{number total steps}}. \tag{7}$$

A good choice for a_r is in the range $0.3 < a_r < 0.5$ [11]. A snapshot of a fluctuating membrane (in the absence of particles) can be visualized in Fig. 4.
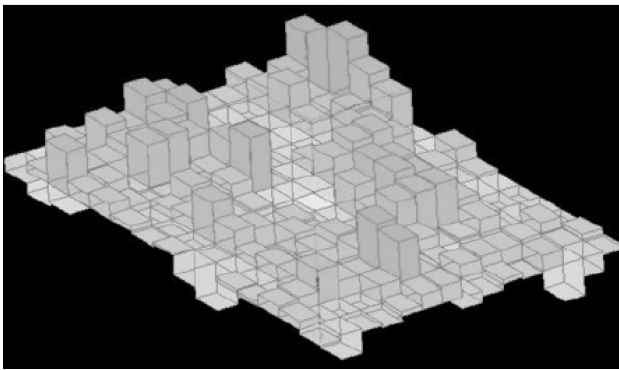
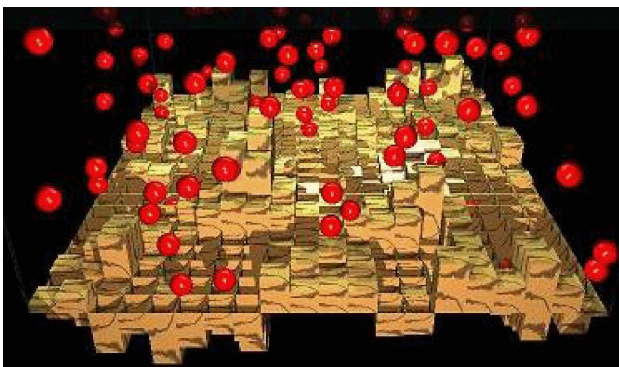FIGURE 4. Snapshot of a fluctuating membrane.

FIGURE 5. Snapshot of the membrane-colloid system.

3.2. Simulating colloidal particles in contact with a fluctuating membrane

Now, we shall describe the simulation details for the particles which interact with the membrane (see Fig. 5). A colloidal particle is represented by a sphere of diameter σ, and its position is given by the coordinates (x, y, z). We place the membrane inside a harmonic potential located at $z = 0$. The N colloids are then randomly distributed between the membrane and a flat wall located at $z = d$, where d is chosen such that the direct membrane-wall interaction can be neglected, *i.e.* $d \gg \xi_\perp$. Similar to the membrane, colloidal particles are moved to a new configuration by means of random displacements, $x_i = x_i + x_{max}(\text{rand}() - 0.5)$, where x_{max} is the maximum step size of the colloids which is updated after every certain number of Monte Carlo steps. If two particles overlap ($r_{ij} < \sigma$, where r_{ij} is the distance between two cores) or if one of the spheres penetrates the membrane ($z_{ij} - \sigma/2 < h_{ij}$, where z_{ij} is the z-coordinate of the particle located on the h_{ij} lattice), we reject the proposed configuration. Subsequently, the energy of the new configuration is calculated according to (1). The simulating algorithm can be summarized as follows:

1. Locate a fluctuating membrane at $z = 0$.

2. Locate a hard-wall at $z = d$. The separation between the fluctuating membrane and the second flat wall is

adjusted according to the desired density and the requirement $d \gg \xi_\perp$.

3. Place N colloidal particles randomly between the membrane and the wall.

4. Move the membrane to a new configuration and determine if this configuration is accepted or rejected; if the configuration is accepted, update the new coordinates of the membrane sites.

5. Move the colloidal particles to a new configuration and determinate if this configuration is accepted or is rejected; if it is accepted, update the new coordinates for every particle.

6. Calculate the acceptance ratio of the membrane and the colloids.

7. Update h_{max} and x_{max}.

8. Calculate the observables.

9. Return to step 4.

The distance, r, between a colloid with diameter σ located at $\mathbf{R}_1 = (\mathbf{r}_1, \mathbf{z}_1)$ and a membrane site at $\mathbf{R} = (\mathbf{r}, h(\mathbf{r}))$ is given by (see Fig. 6)

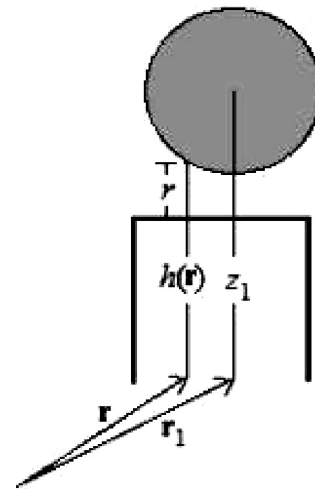$$r = \sqrt{(\mathbf{r} - \mathbf{r}_1)^2 + (z_1 - h(\mathbf{r}))^2} - \frac{\sigma}{2}. \qquad (8)$$

FIGURE 6. Distance r between a colloid with diameter σ, located at $\mathbf{R}_1 = (\mathbf{r}_1, z_1)$n and a membrane site at $\mathbf{R} = (\mathbf{r}, h)$. For point-particles, $r = z_1 - h(\mathbf{r})$.

FIGURE 7. Squematic representation of the approximation used to determine if a particle penetrates the membrane.
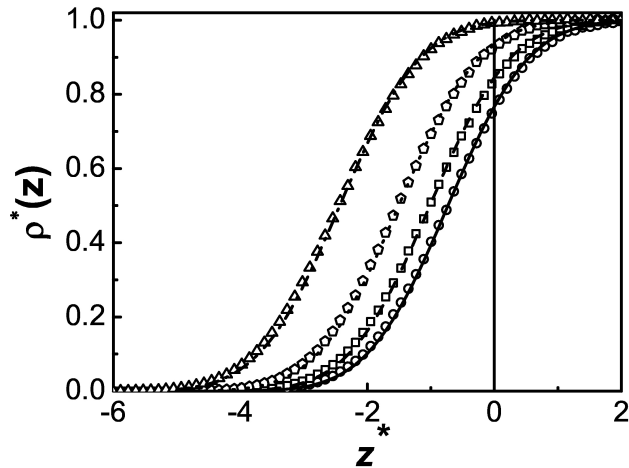
FIGURE 8. Density profile, $\rho^*(z) = \rho(z)/\rho_\infty$, for four different reduced densities, from right to left $\rho_\infty \xi_\perp^3 = 0.01139, 0.01587, 0.02351$ and 0.03803. Distances are scaled with $\xi_\perp$, then $z^* = z/\xi_\perp$. Symbols correspond to simulation data and lines to Eq. (13). The perpendicular line at $z^* = 0$ is just a guide for the eye to illustrate the deviation of the profile with increasing in the particle density.
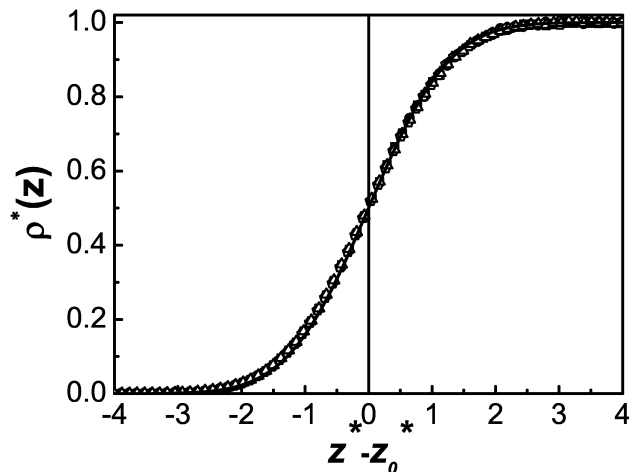

FIGURE 9. Master curve. These are the same curves as in Fig. 8, but now all curves have been plotted as functions of $z - z_0$. Solid line is obtained from Eq. (13). The perpendicular line at $z^* - z_0^* = 0$ is just a guide for the eye to illustrate the symmetry of the master profile.

In order to save CPU time, the colloid close to the membrane surface is approximated by a cube (see Fig. 7); the actual minimal height difference depends on the distance between the centers of the colloids and the lattice site.

4. Density profile: comparison with the point-like particle limit

We now consider N colloidal particles of diameter σ in contact with the membrane. Their positions are characterized by the vectors $\vec{r}_i$, $i = 1, \ldots, N$. They interact each other

through the hard-core potential described by the relation

$$\beta u_{cc}(r) = \left\{ \begin{array}{ll} \infty & r < \sigma \\ 0 & r \geq \sigma, \end{array} \right. \tag{9}$$

where r denotes the relative distance between colloids, $r = |\vec{r}_i - \vec{r}_j|$. The colloid-membrane interaction is given by

$$\beta u_{cm}(\vec{r}_i) = \left\{ \begin{array}{ll} +\infty & r < 0 \\ 0 & r \geq 0, \end{array} \right. \tag{10}$$

where r is given by Eq. (8). Therefore, the Hamiltonian of the system can be expressed as

$$H = H_m + H_{cc} + H_{cm}, \tag{11}$$

where H_m is given by Eq. (1) and H_{cc} and H_{cm} are the colloid-colloid and colloid-membrane Hamiltonians, respectively. Then, the partition function can be written as

$$Z = \frac{1}{\lambda^{3N} N!} \int d\vec{r}_1 \ldots d\vec{r}_N \int Dh e^{-\beta H_m(h)} e^{-\beta \sum_{i=1}^{N} u_{cm}(\vec{r}_i)}$$
$$\times e^{-\beta \sum_{j>i}^{N} u_{cc}(r_{ij})}, \tag{12}$$

where λ, which results from the integration over the particle momenta, is the so-called thermal wavelength. The functional integral extends over all configurations of the field h, weighted with the Helfrich Hamiltonian (1). The positions of the particles are restricted by the membrane.

In general, the analytical integration of the partition function is a hard task which has been simplified in a few cases. In particular, for the case of a system composed of point-like particles ($\sigma = 0$), the partition function (12) has been analytically calculated by Bickel *et al.* [6]. Therefore, once the partition function is computed one is able to calculate any physical observable.

Then, the density profile of point-like particles in front of a fluctuating membrane reads as [6]

$$\rho(z) = \rho_\infty \times \frac{1}{2} \left[1 + \mathrm{erf}\left(\frac{z + z_0}{\sqrt{2}\xi_\perp} \right) \right], \tag{13}$$

where ρ_∞ is the bulk density and z_0 is the characteristic length $z_0 = \rho_\infty \hat{\mu}^{-1}$. The physical meaning of this length can be understood as follows. When in contact with the colloidal suspension, the membrane experiences the osmotic pressure of the particles and the membrane moves to a new equilibrium position given by z_0. Therefore, Eq. (13) provides an excellent benchmark to test our simulation model described above.

Figure 8 shows the density profile, $\rho(z)/\rho_\infty$, for four reduced densities, $\rho_\infty^* \equiv \rho_\infty \xi_\perp^3$. Symbols correspond to the simulation data and solid lines to the expression given by Eq. (13). We can observe a perfect agreement between both simulations and theory. From the curves, we appreciate that the displacement z_0 increases with the density according to the relation $z_0 = \rho_\infty/\hat{\mu}$. Therefore, it is possible to have a master curve if all curves are plotted as function of $z - z_0$.

Figure 9 shows the master curve obtained from our simulation data and the corresponding analytical expression given by Eq. (13). From this curve, we appreciate the fact that the effect of the particles on the membrane is to modify the mean surface location without changing the topology of the membrane. On the other hand, up to here it is possible to compare our simulations with analytical expressions, and the next step is to consider particles with a finite size; in case it is not possible to analytically integrate the partition function, and so our simulation method becomes a very powerful tool in facing this problem. Results in this direction will be published elsewhere [13].

5. Conclusions

We have introduced a model to simulate a system composed of hard-colloidal particles in contact with fluctuating membranes. The latter are described by means of the Helfrich Hamiltonian. We tested our model at the limit of point-like particles where the analytical expression for the density profile makes it possible to show the accurateness of our simulation method. We found that our results are in perfect agreement with this.

Finally, we would like to emphasize the fact that the model described here can be used to study the effect of finite size colloids on both the structural and thermodynamic properties of hard-colloidal particles close to fluctuating walls. Also, such a model can easily be extended to binary systems in order to investigate the effect of thermal fluctuations on the wall-particle depletion potentials, or to systems with long-range (Coulomb-like) interactions.

Acknowledgments

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