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Abstracting the essence of the confinement effect on crowding microspheres: Mean-field theory and numerical simulation

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ABSTRACT

We investigate a mean filed theory to elucidate the fraction of hard spheres in the rim of rigid spherical cavities for densities similar to crowded cellular nuclei. Rims are one hard sphere thickness from the interior surface of cavities. We theoretically interpret the particle fraction around the rim by considering entropies from inter-particle excluded volume interactions and depletion forces under confined cavities. By adapting the characteristic length of depletion forces as a single tunable parameter, the proposed theory is successfully applied to understand simulation data, which provides a simple but general picture on confinement effects including cavity curvature and density.

1. Introduction

Biological cells are highly crowded, and in their nuclei, genome materials and proteins take up around 30% of the entire cell volume [1,2]. The macromolecular crowding inside the cell accounts for distinct disparities between biochemical measurements *in vitro* and *in vivo* [3, 4, 5]. Technical difficulties impede detailed understanding of the material properties and chemical processes in the tiny nucleoplasm. The recent experimental advancement, however, has rendered new pictures at the level of nuclei; as a result, differentiable features can be observed between normal and cancerous cells [6,7]. The nuclei of normal human cells showed a prominent rim around their edges, whereas those cancerous counterparts had diminishing rims around nuclei. These novel findings have motivated our work to investigate the rim density for particles with relative high densities being confined within cavities.

From the standpoint of molecular interactions, excluded volume interactions among cellular materials are essential under macromolecular crowding, and entropies may have significant influences on the spatial distribution of cellular materials. To address the effect of entropy on structural specificity under crowding confinement, one-component confined hard sphere fluids are studied prior to exploring more complex models. Such a model allows us to elucidate the essential role of two competing entropic forces for confined particles: one is the inter-particle excluded volume interaction and the other is the depletion force arising from the interaction between particles under confined cavities.

The effort over past theoretical developments has enabled structure calculations of confined liquids in rigid spherical cavities, in particular, by using density functional theory. For the one-component hard sphere liquid in spherical cavities, density functional theory has provided detailed information, including cavity induced depletion forces [8, 9, 10]. Despite its success, it is instructive to devise alternative approaches to investigate the structure of hard sphere liquids by which we are able to reconstruct the structural information of confined particles through intuitive entropic descriptions, for example. The more intuitive approach is beneficial to provide clear physical pictures regarding the role of various entropic forces on structural determination. This is crucial for future model designs to understand more complex fluids containing multiple components under confinement as in realistic biological cells.

In this work, we report our investigation on the rim density of hard sphere fluids within the rigid spherical cavity by using two approaches: (1) large-scale Monte Carlo simulations up to 19200 particles and (2) a mean field theory by combing the entropic forces due to inter-particle excluded volume interactions along with depletion forces arising from the spherical cavity. The direct comparison between these two approaches is expected to validate the performance of the mean field theory, with focus on higher particle densities to mimic crowded and large cellular nuclei.

2. A mean field model

The investigated model (in 3D) consists of one-component dense hard spheres of diameter σ confined within a rigid spherical cavity of radius R_{cav}, of which 2D schematic plot is shown in Figure 1. Our main focus is on the case when hard sphere particles

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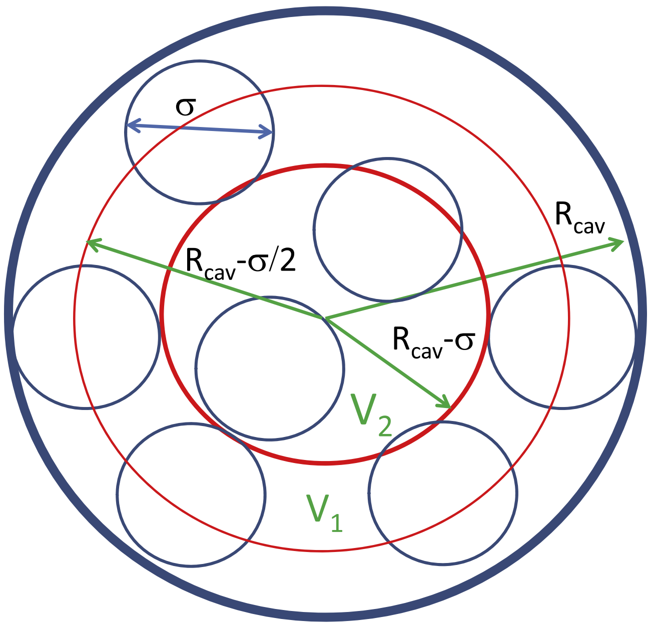

Figure 1. The 2D schematic of the investigated model (in 3D) consisting of N hard spheres of diameter σ confined in the spherical cavity of radius R_{cav} divided into two regions: (1) adsorption layer (rim region: $[R_{cav}-\sigma, R_{cav}-\sigma/2]$) of volume V_1 along with N_1 particles (2) central region with volume V_2, separated by the radial distance $R_{cav}-\sigma$.

occupy up to 30% of the cavity volume, and such a value is motivated by the crowded nucleus within a realistic biological cell. The center of particles is allowed to effectively move in the radial range between zero and $R_{cav}-\sigma/2$, considering the hard core repulsion of spherical particles and the cavity. We are interested in calculating the fraction of particles distributed in the layer between $R_{cav}-\sigma$ and $R_{cav}-\sigma/2$ around the interior surface of the spherical cavity, which is within the first 'adsorption' layer induced by the depletion forces between particles and the cavity surface as well as the crowding effect among particles under investigated densities. The particle fraction in this region is analogous to the rim density of genome materials around the interior surface of a nucleus. In one-component hard sphere fluids, the fraction of the cavity volume occupied by N hard spheres is equivalent to the packing fraction, $\eta = \frac{N\sigma^3}{8R_{cav}^3}$.

In the model, we divide the confined spherical cavity into two regions: (1) 'adsorption' layer (rim region) $r \in [R_{cav}-\sigma, R_{cav}-0.5\sigma]$ with volume V_1 (no particles centered in $r \in [R_{cav}-0.5\sigma, R_{cav}]$); (2) central region: $r \in [0, R_{cav}-\sigma]$ with volume V_2. The number of particles in these two regions is given by N_1 and N_2, respectively, and the total number of particles N equals $N_1 + N_2$. For hard sphere fluids, the system is exclusively dominated by entropy. In our mean field model, the entropy of the system is divided into the following two parts.

(A) Depletion forces from cavity boundaries

To better understand the entropy effect due to confined boundaries, we first investigate the free volume due to two interacting hard spheres, as shown in Figure 2. In Figure 2, a hard sphere is placed at a radial distance z from the center of the spherical cavity. The excluded volume $V_{excl}(z)$ is given by

$$V_{excl}(z) = \frac{\pi}{24z^3}\Big\{[6zR_{eff}-\sigma^2+(z-R_{eff})^2][\sigma^2-(z-R_{eff})^2] + [(6\sigma R_{eff}-R_{eff}^2+(R_{eff}-\sigma)^2][R_{eff}^2-(z-\sigma)^2]^2\Big\} \text{ if } z \geqslant R_{cav}-1.5\sigma \quad (1)$$

$$= \frac{4\pi\sigma^3}{3} \quad \text{if } 0 < z < R_{cav}-1.5\sigma \quad (2)$$

where $R_{eff} = R_{cav}-0.5\sigma$. In the limiting case when $z = R_{eff}$, $V_{excl}(z = R_{eff}) = \frac{2\pi}{3}\sigma^3 - \frac{\pi\sigma^4}{4R_{eff}}$. As $R_{eff} \to \infty$, the limiting V_{excl} is

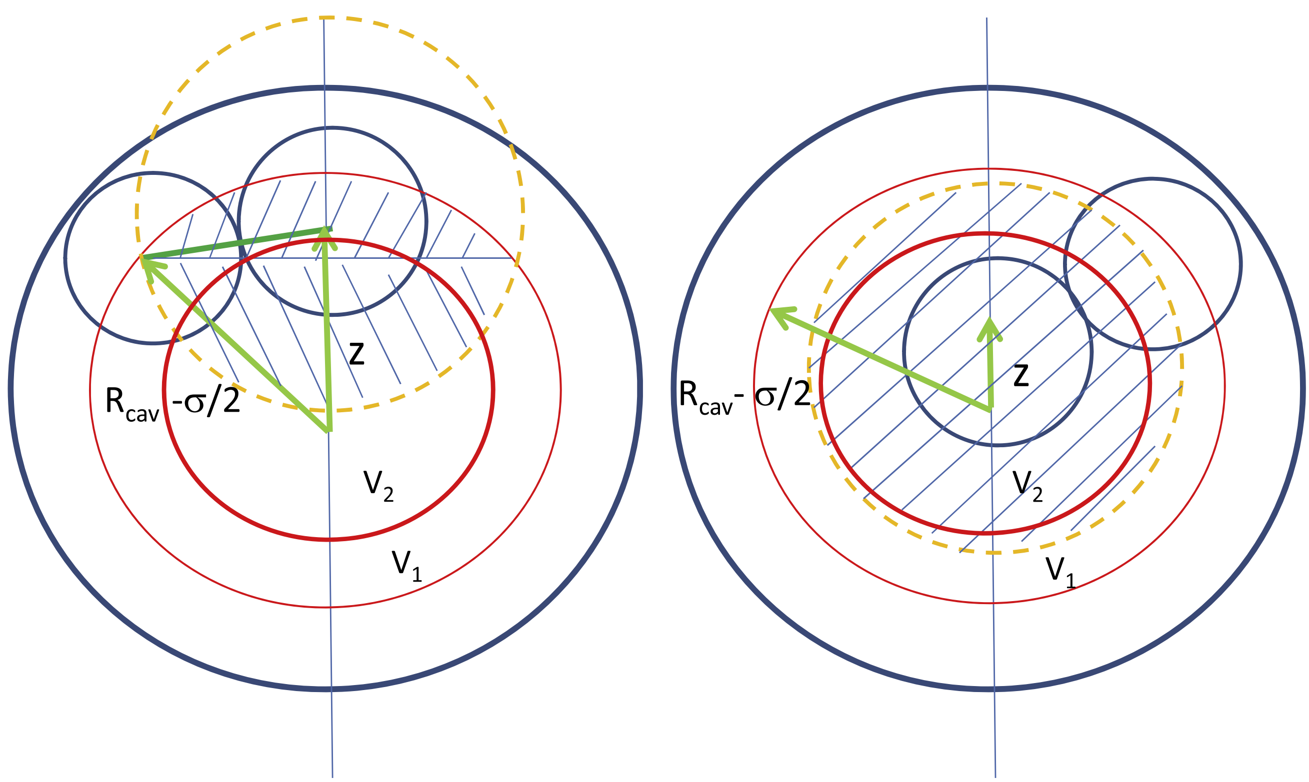

Figure 2. The 2D representation of the excluded volume (shaded area) between two hard spheres in a spherical cavity (in 3D), where $R_{cav}-3\sigma/2 < z < R_{cav}-\sigma/2$ for the left figure and $z > R_{cav}-3\sigma/2$ for the right figure.