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Shape change of nano-containers via a reversible ionic buckling

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We demonstrate that small charged nano-cages can undergo reversible changes of shapes, by modifying the ionic conditions including salt concentration, pH and dielectric permittivity of the medium. Using numerical simulations, we analyze structures with various charge stoichiometric ratios. At zero or low charge densities, the shape of the cage is determined by its elastic properties, and the surface charge pattern is dictated by the globally fixed geometry. As the charge density per molecule increases, the shape is strongly affected by the electrostatic forces. In this regime, the shape of the nano-cage is controlled by the charge distribution.

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A reversible control of shape and deformability of nano-scale objects is of great importance in a variety of technological problems and biological processes. Examples include metallic nano-cages [1], spectrin-based network in red blood cells [2, 3], lamin-based nuclear meshworks in eukaryotic cells [4], and carboxysomes present inside some bacteria [5]. The size and shape of metallic nano-cages determine their ability to absorb and scatter light, making them ideal candidates for smart contrast agents in medical imaging [6, 7]. Flexibility of spectrin networks is essential for the ability of a red blood cell to pass through capillaries: it is achieved via protein structural changes [8] that govern its elastic properties [9]. The shape and mechanical properties of the lamin meshwork are important for a number of nuclear cell functions [4, 10]. Carbon fixation by carboxysomes [11] confirms to a large extent how the function of a nano-container is determined by its shape. Here we show that electrostatic interactions can greatly influence the shape in a controllable and reversible fashion.

One important goal of nanotechnology is to construct biomimetic nano-compartments with properties, like size and shape, that can be easily regulated by external parameters, such as solvent quality, pH and/or salt concentration, and do not require modifications in the chemical composition of the container. Understanding how to control the shape is not only of a fundamental importance for designing novel nano-containers, but it is also an example of an emergent phenomenon. Using a minimal coarse-grained model, we argue that electrostatic interactions can drive reversible shape changes in small nano-cages with oppositely charged components. By comparing the lowest energy configurations of spherical and icosahedral ionic shells, a recent study [12] demonstrated that electrostatic interactions can trigger a faceting transition. In this paper, we extend that approach by allowing the container to relax its shape and explore how electrostatics affects its optimal conformation. We focus only on small structures, where the charge screening effects are negligible and electrostatic effects are expected to dominate over thermal fluctuations.

We model the nano-container as a hollow shell made of discrete lattice points placed on a spherical surface. The surface points are assumed to form a triangular lattice constructed via the Caspar and Klug construction for spherical viruses [13]. Such lattices are described by a pair of integers, (p, q) which determines the number of lattice points $N = 10T + 2$, where the T -number is defined by $T = p^2 + q^2 + pq$. In this construction, there are exactly 12 lattice points with five nearest neighbors placed on the vertices of an icosahedron. All other lattice sites have coordination number equal to six.

Rather than studying a particular system, we are interested in the qualitative description of the effects of electrostatics on the shape of a nano-sized container. We suppress all atomistic details and instead use a coarse-grained approach. The total energy of the container depends on its shape and is the sum of elastic and electrostatic contributions, $E = E_{el} + E_{es}$. The elastic contribution controls the mechanical properties of the container, that is, its resistance to shape changes. It is modeled using linear elasticity as a sum of the harmonic stretching energy, $E_s = \frac{1}{2}k(r_{ij} - l_0)^2$ and the bending energy $E_b = \kappa(1 + \cos\phi)$ [14], where k is the elastic spring constant, r_{ij} is the distance between two neighboring lattice points, l_0 is the length of an unstretched edge, κ is the bending rigidity, and ϕ is the dihedral angle between two triangles sharing an edge. The electrostatic energy contribution between any two lattice points is given by the standard Coulomb law, $E_{es} = \alpha \frac{Z_i Z_j}{r_{ij}}$, where Z_i is the integer valence of the lattice point i , and α is a parameter with the units of *energy* $\times$ *length*. The quantity α can be interpreted as the Bjerrum length multiplied by the unit of energy, $k_B T$. In this study, we treat α as a tunable parameter that controls the strength of the electrostatic interaction relative to the elastic rigidity of the container. For simplicity, we set the numerical values of the spring constant k and the bending rigidity κ to one, keeping in mind that these quantities have dimensions of *energy/area* and *energy*, respectively. The $1/r$ -form of the Coulomb interaction assumes that the electrostatic interaction propagates in all three dimensions, through

the interior of the shell. We ignore any dielectric heterogeneities and assume that the cage wall as well as its interior and exterior have identical dielectric properties, effectively parametrized by α . Finally, to prevent the electrostatic collapse of neighboring sites, we have assigned a radius $r = 0.35l_0$ to each lattice point, modeled as a hard-core repulsive potential.

We focus on small structures with T -number up to 9 (i.e., $(p, q) = (2, 1)$) and approximately 50 lattice points. For a 15nm nano-cage, each lattice point roughly corresponds to 15-20 atoms. Starting from a charge-neutral spherical configuration with a random distribution of charges, we find an optimal shape using simulated annealing Monte Carlo simulations. A Monte Carlo move consists of two steps: (1) the random displacement of a vertex is attempted, followed by (2) an attempt of swapping charges of a randomly chosen pair of vertices. In both steps, moves are accepted according to the Metropolis algorithm. Typically, we used ten cooling/reheating cycles with a linear cooling protocol and computed the optimal shell volume by averaging over minimum energy configurations for each cycle. To fully relax the shape, one million Monte Carlo sweeps were used in each cooling cycle, with a sweep defined as a number of moves equal to the number of lattice sites. The requirement of charge neutrality puts a constraint on possible T -numbers that are compatible with a particular charge ratio. We choose a (p, q) -pair with the smallest T -number compatible with that ratio. In our model, the unstretched edge length l_0 is chosen as a unit of length. Consequently, nano-containers with different T -numbers have different, but comparable, radii between $1.5l_0$ to $2.2l_0$. Although the Caspar-Klug construction defines a regular triangular lattice on the faces of an icosahedron, the lattice is distorted when radially projected on the surface of a sphere. Unlike in Ref. [12] where it was necessary to construct a projection that produces a uniform distribution of vertices on the sphere, here this is not the case as all initial distortions quickly relax due to elastic forces. Thus, a simple gnomonic projection suffices. Finally, we point out that no triangular lattice on a sphere can have all edges of equal length l_0 , which results in a finite residual stretching energy even in the relaxed lattice. For large systems, this can lead to spontaneous buckling [17]. However, for small uncharged containers, the bending energy wins, and the shape remains spherical.

In Figure 1 we show snapshots of the relaxed shapes of nano-containers with the charge ratios of $Z_+ : Z_- = 1 : 1$ to $7 : 1$. We note that no Caspar-Klug lattice is compatible with a $Z_+ : Z_- = 4 : 1$ electroneutral system [12]. For weak electrostatic interaction, the containers shrink, lose their spherical shape and become oblique. The charges rearrange on the surface in a pattern that minimizes the Coulomb energy. If the electrostatic interaction is increased beyond a non-universal critical value that depends on the cage size and the charge ratio, Coulomb at-

FIG. 1: (color online) Relaxed configurations of small nano-containers as a function of the strength of the electrostatic interaction α for six charge ratios of $Z_+ : Z_- = 1 : 1$, $2 : 1$, $3 : 1$, $5 : 1$, $6 : 1$, and $7 : 1$, and (p, q) -pairs: $(1, 1)$, $(2, 0)$, $(1, 1)$, $(2, 0)$, $(2, 0)$, and $(2, 1)$ (rows, top to bottom). Left hand side labels indicate the charge ratio in each row; labels on the right are sizes of the uncharged reference shells. Note that no Caspar-Klug lattice is compatible with $4 : 1$ charge ratio. As the strength of the electrostatic interaction is increased (moving left to right within a row), the change in shape is immediately apparent. Initially, the nano-cage contracts, reduces its volume, and transforms into an oblique shape. Beyond a non-universal critical strength α_c the container collapses (right most column). Values of α are not the same within one column and are instead chosen to best represent the shape for that particular charge ratio. Positive charges are shown in red, negative in blue and the yellow mesh represents the reference shape of the uncharged container. Snapshots are produced using Visual Molecular Dynamics (VMD) package [15] and rendered with Tachyon ray-tracer [16].

traction fully overcomes the elasticity, and the container collapses, as shown in the rightmost column in Figure 1.

In order to quantify the shape change, in Figure 2 we plot the relative volume change V/V_0 (with respect to the reference volume V_0 of an uncharged container) as a function of the normalized strength of the electro-

static interaction. The cage volume is calculated as [18] $V = 1/6 \sum_T |\vec{r}_{T,1} \cdot (\vec{r}_{T,2} \times \vec{r}_{T,3})|$, where $\vec{r}_{T,1}$, $\vec{r}_{T,2}$, and $\vec{r}_{T,3}$ are three vertices of the triangle T , and the sum runs over all triangles on the surface. Even a very weak electrostatic interaction, e.g., $\alpha Z_+/R \approx 0.2$, where Z_+ is the valence of positive charges and R is the radius of the uncharged reference cage, leads to a sizable change of the volume, reducing it to $\approx 0.4 - 0.6V_0$. As the strength of the Coulomb interaction is increased beyond $\alpha Z_+/R \approx 0.2$, the container almost stops shrinking, and for a range of values of α , it remains essentially constant. If the electrostatic interaction is increased further above a critical value, one observes a sharp drop in the volume, indicating a collapse of the structure. The onset of the electrostatic collapse is very sensitive to the charge ratio, and as $Z_+ : Z_-$ is increased, the parameter region over which the container is stable reduces rapidly. For example, a 1 : 1 container remains inflated until very large values of α , while a 7 : 1 cage collapses almost immediately after a very narrow region of stability. In the case of a small Z_+ , a small number of negative charges is needed to screen its effects over long distances. On the other hand, a high-valence positive charge is harder to screen, and its effects are felt over the whole container. During the initial deflation, oppositely charged neighbors are attracted toward each other, thereby decreasing the inter-particle distance while increasing the stretching energy. However, there is very little change of the bending energy. For small charge ratios, this process continues until the neighboring sites cannot come any closer to one another due to the hard core repulsion, while for large valences the deflation is additionally limited by repulsion of the strong positive charges. This accounts for the observation of somewhat larger values of V/V_0 for large charge ratios. Resistance to bending is the main force that prevents the collapse. Once the electrostatic forces become strong enough to overcome the bending barrier, the whole cage crumples. Due to the very small size of the studied containers any asymptotic scaling analysis of the energy scales would be hard to justify. Instead, in the Supporting Information we include a brief discussion based on simulation results about the competition between elastic and electrostatic energies. Finally, we note that close to the point of collapse V/V_0 fluctuates, which we attribute to the limitations of the simulated annealing minimization technique to find an absolute energy minimum in a very rough energy landscape, as is expected close to the collapse. Instead, the system gets trapped in a local minimum.

Electrostatic collapse is accompanied with a substantial reorganization of charge on the cage surface. In order to quantify this effect we computed the charge-charge correlation function, $C(r) = \frac{1}{N} \sum_i \sum_{j \neq i} \frac{1}{\Delta v(r)} q(\vec{r}_i) q(\vec{r}_j)$, where $q(\vec{r}_i)$ is charge at position $\vec{r}_i$, $\Delta v(r)$ is the volume of a spherical region of radius r and thickness Δr (i.e., the center of the corre-

FIG. 2: (color online) Volume change of the nano-cage as a function of the strength of the electrostatic interaction for charge-neutral cages with six different charge ratios. To simplify comparison between different cases, we have normalized the electrostatic strength by the radius R of uncharged cage (thus, the ratio $\alpha Z_+/R$ has units of energy). Even a weak electrostatic interaction leads to a rapid change in the volume, and for $\alpha Z_+/R \approx 0.2$, the cage shrinks to about 40-60% of its uncharged size. As the strength of the Coulomb interaction is increased, the volume change reaches a plateau. Over a range of values of $\alpha Z_+/R$ the volume essentially does not change. Finally, a threshold is reached, the electrostatic attraction fully overcomes any elastic forces and the cage collapses. The onset of the collapse moves to the lower values of $\alpha Z_+/R$ with the increase in the charge ratio $Z_+ : Z_-$. V_0 is the reference volume of the spherical cage with no electrostatic interaction and Z_+ is the valence of the positive charges ($Z_- = 1$ for all cases).

sponding histogram bin and its width, respectively), and N is the total number of charges. In Figure 3 we show the charge-charge correlation function for three different stoichiometric ratios at three values of the electrostatic strength, i.e., in the region where the shell shrinks, at the plateau, and above the collapse, as shown in Figure 2. It is evident that the change in containers shape leads to a substantial reorganization of the surface charge. This effect is particularly prominent in the collapsed state. The observed charge reorganization would further complicate any analytic analysis of the problem.

The present discussion is limited to small containers, in the 10 – 15nm size range, where the discrete nature of the embedded charges is important and the electrostatic effects are strong over the whole size of the shell. For large vesicles with small charge ratios, electrostatic effects are most important locally, leading to a number of qualitatively different effects. For example, in a mixture of charged lipids, strong local electrostatic interaction can lead to the crystallization of lipid tails with profound effects on the vesicle shape [19].

In summary, using Monte Carlo simulations of a coarse grained model for nano-size hollow containers with embedded charges, we showed that the electrostatic inter-

FIG. 3: (color online) Charge-charge correlation function $C(r)$ as function of the strength of electrostatic interaction $\alpha Z_+/R$ for three stoichiometric charge ratios: 1:1 (top), 1:3 (middle) and 1:7 (bottom). Values of $\alpha Z_+/R$ are chosen to be: in the shrinking region (solid), in the middle of the plateau (dashed), and above the cage collapse (dotted), as shown in Figure 2. Changes of features of the charge-charge correlation function are clearly evident indicating a significant charge reorganization on the shell surface as $\alpha Z_+/R$ is increased. $R = 1.5l_0$, $1.7l_0$ and $2.2l_0$ (top to bottom) are radii of uncharged reference shells.

action can lead to reversible changes in the container shape. We found that a weak electrostatic interaction can lead to an appreciable change in the volume and the overall shape, which can result in changes of optical properties of the container, for example. Furthermore, the electrostatic interaction could be tuned by changing such properties as pH and salt concentration of the surrounding solvent, or by shining light of an appropriate wave length onto the container. Even in the very low salt concentration regime, where the present analysis is applicable, a change in $pH - pK_a$ from 0 to 4 could lead to approximately two fold increase in the degree of dissociation [20, 21]. The resulting change of the local charge should be sufficient to trigger observable changes of the cage volume as predicted in Figure 2 for small values $\alpha Z_+/R$. A similar, although slightly weaker effect [20] would be expected as a function of the screening length tuned by changing the salt concentration. On the other hand, accessing the electrostatic collapse of the cage at large electrostatic strengths, $\alpha Z_+/R \gtrsim 3$ would be much harder to realize experimentally.

The proposed mechanism could provide a tool for building intelligent nano-containers with properties that could be easily controlled over a considerable range of

shapes and sizes. This would eliminate the need to synthesize new containers each time a different size or shape is required. However, a real challenge would be to synthesize nano-cages with the precise charge distributions similar to those assumed in our model.

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