Supplementary Information

Osmotic stress and pore nucleation in charged biological nanoshells and capsids

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I. FMT IN SPHERICAL GEOMETRY

We now provide explicit formulas for the FMT weighted densities in the underlying spherical geometry. The scalar weighted densities used in the hard-sphere functional can be written as

$$n_\alpha(\boldsymbol{r}) = \sum_i \int \rho_i(\boldsymbol{r}')\omega_\alpha^{(i)}(\boldsymbol{r}-\boldsymbol{r}')d\boldsymbol{r}'. \tag{1}$$

Here, the subscript α denotes the set of weighted function, whereas the upper index (i) refers to the ionic spices. The weight functions can be either scalar or vector entities. The scalar ones are given by

$$\omega_3^{(i)}(\boldsymbol{r}) = \Theta(a_i - r) \tag{2a}$$

$$\omega_2^{(i)}(\boldsymbol{r}) = \delta(r - a_i) \tag{2b}$$

$$\omega_1^{(i)}(\boldsymbol{r}) = \frac{\omega_2^{(i)}(r)}{4\pi a_i} \tag{2c}$$

$$\omega_0^{(i)}(\boldsymbol{r}) = \frac{\omega_2^{(i)}(r)}{4\pi a_i^2}. \tag{2d}$$

The subscript α is such that $(\alpha-3)$ refers to the spatial dimensionality of the underlying weighted density. The vector weighted densities are represented as convolutions similar to the ones in Eq. (1), with the weight functions replaced by the following vectors:

$$\boldsymbol{\omega}_2^{(i)}(\boldsymbol{r}) = -\nabla\omega_3^{(i)}(\boldsymbol{r}) = \delta(r - a_i)\hat{\boldsymbol{e}}_r \tag{3a}$$

$$\boldsymbol{\omega}_1^{(i)}(\boldsymbol{r}) = \frac{\boldsymbol{\omega}_2^{(i)}(\boldsymbol{r})}{4\pi a_i}, \tag{3b}$$

where $\hat{\boldsymbol{e}}_r = \boldsymbol{r}/r$ is the unit vector pointing at the radial direction. In the present situation of radially symmetric potentials, the density profiles depend only on the radial coordinate r'. Likewise, the scalar weight functions depend only on the relative distance $R = |\boldsymbol{r} - \boldsymbol{r}'| = \sqrt{r^2 + r'^2 - 2\boldsymbol{r}\cdot\boldsymbol{r}'}$ between source and observation points.

The integrals in (1) can therefore be explicitly written as

$$n_\alpha(\boldsymbol{r}) = \sum_i \int_0^\infty \rho_i(r') r'^2 dr' \int_0^{2\pi} d\varphi' \int_0^\pi \omega_\alpha^{(i)}(R) \sin\theta' d\theta'. \tag{4}$$

If we now conveniently set the z-axis along the direction of the observation point $\boldsymbol{r}$ in performing the above integral, the relative distance R becomes $R = \sqrt{r^2 + r'^2 - 2rr'\cos\theta'}$. Integration over the azimuthal angle φ' can be readily performed, while the integration over polar angle θ' can be converted into an integral over the relative distance R. To this end, we note that $RdR = \dfrac{\sin\theta'}{rr'} d\theta'$. Converting the integration limits accordingly, we arrive at the following result for the scalar weighted densities:

$$n_\alpha(r) = \frac{2\pi}{r} \sum_i \int_0^\infty r' \rho_i(r') dr' \int_{|r-r'|}^{r+r'} \omega_i^{(\alpha)}(R) R dR. \tag{5}$$

A similar reasoning can be applied to rewrite the vector weight densities

$$\boldsymbol{n}_\alpha(r) = \sum_i \int \boldsymbol{\omega}_\alpha^{(i)}(\boldsymbol{r} - \boldsymbol{r}') \rho_i(\boldsymbol{r}') d\boldsymbol{r}' \tag{6}$$

into a much simplified form. We first notice that the vector weight functions in Eqs. (3a) and (3b) can be written as $\boldsymbol{\omega}_\alpha^{(i)}(\boldsymbol{r} - \boldsymbol{r}') = |\boldsymbol{\omega}_\alpha^{(i)}(R)| \hat{\boldsymbol{e}}_R$, where $\hat{\boldsymbol{e}}_R = \frac{(\boldsymbol{r} - \boldsymbol{r}')}{R}$ is the unit vector connecting integration and observation points. The integrals above can thus be explicitly written as

$$\boldsymbol{n}_\alpha(r) = \sum_i \int_0^\infty \rho_i(r') r'^2 dr' \int_0^\pi \sin\theta' d\theta' \int_0^{2\pi} \frac{|\boldsymbol{\omega}_\alpha^{(i)}(R)|}{R} (\boldsymbol{r} - \boldsymbol{r}') d\varphi'. \tag{7}$$

Once again, it is convenient set the (fixed) radial vector $\hat{\boldsymbol{e}}_r$ as pointing along the z-axis, $\hat{\boldsymbol{e}}_z$, while performing the above integral. With this choice, the integration source point $\boldsymbol{r}'$ can be composed in terms of its cartesian components as

$$\boldsymbol{r}' = r'(\sin\theta'\cos\varphi'\ \hat{\boldsymbol{e}}_x + \sin\theta'\sin\varphi'\ \hat{\boldsymbol{e}}_y + \cos\theta'\ \hat{\boldsymbol{e}}_z), \tag{8}$$

while $\boldsymbol{r} = r\hat{\boldsymbol{e}}_r = r\hat{\boldsymbol{e}}_z$. It is easy to check that contributions in the x and y directions will vanish when the above expression is inserted into Eq. (7), since the azimuthal integrals are zero. Only the contribution along the z-axis (which coincides with the $\hat{\boldsymbol{e}}_r$ direction) survives, and a simple integration over the azimuthal angle provides

$$\boldsymbol{n}_\alpha(r) = 2\pi\hat{\boldsymbol{e}}_r \sum_i \int_0^\infty \rho_i(r') r'^2 dr' \int_0^\pi \frac{|\boldsymbol{\omega}_\alpha^{(i)}(R)|}{R} (r - r'\cos\theta') \sin\theta' d\theta'. \tag{9}$$

The second integral over polar angle can be again transformed into an integral over the relative distance R, under the simple replacement $\cos\theta' = \dfrac{r^2 + r'^2 - R^2}{2rr'}$. The above integral assumes then the form

$$\boldsymbol{n}_\alpha(r) = \frac{\pi}{r^2}\hat{\boldsymbol{e}}_r \sum_i \int_0^\infty r'\rho_i(r') dr' \int_{|r-r'|}^{r+r'} |\boldsymbol{\omega}_\alpha^{(i)}(R)| \left[R^2 + r^2 - r'^2\right] dR. \tag{10}$$

It is quite clear from Eqs. (5) and (10) that both scalar and vector weighted densities will be radially symmetric, just like the original densities. Besides, the vector densities always point in the radial direction of the observation point, $\hat{\boldsymbol{e}}_r$. Inserting the weight functions from Eqs. (2b) and (3a) into Eqs. (5) and (10), respectively, leads to the following explicit relations:

$$n_2(r) = \frac{2\pi}{r} \sum_i \int_0^\infty r'\rho_i(r') dr' \int_{|r-r'|}^{r+r'} \delta(R - a_i) R dR \tag{11a}$$

$$\boldsymbol{n}_2(r) = \frac{\pi}{r^2}\hat{\boldsymbol{e}}_r \sum_i \int_0^\infty r'\rho_i(r') dr' \int_{|r-r'|}^{r+r'} \delta(R - a_i) \left(R^2 + r^2 - r'^2\right) dR. \tag{11b}$$

The integrals over the relative distance R will clearly vanish whenever the point $R = a_i$ lies outside the range of integration. If $r > a_i$, this condition is fulfilled for r' in the range $r - a_i \le r' \le r + a_i$ (for the upper integration limit is always bigger than a_i in this case). On the other hand, if $r < a_i$, this condition implies $a_i - r \le r' \le r + a_i$. Thus, only values of r' within these ranges will have a non-vanishing contribution in the first integrals above. Moreover, the delta functions will

simply filter the points $R = a_i$ in these intervals, resulting in the following simplified expressions:

$$n_2(r) = \frac{2\pi}{r} \sum_i a_i \int_{|r-a_i|}^{(r+a_i)} r' \rho_i(r') dr' \tag{12a}$$

$$\boldsymbol{n}_2(r) = \frac{\pi}{r^2} \hat{\boldsymbol{e}}_r \sum_i \int_{|r-a_i|}^{(r+a_i)} r' \rho_i(r') [r^2 + a_i^2 - r'^2] dr'. \tag{12b}$$

There is an apparent singularity in the above weighted functions as one approaches the center of the shell (*i. e.*, at $r \to 0$). However, it is easy to check that the integrals in (12a) and (12b) scale as $\sim r$ and $\sim r^3$, respectively, at this point, so that the weighted densities remain finite at the origin. From the above expressions, explicit relations for the weighted densities $n_0(r)$, $n_1(r)$, as well as for the vector density $\boldsymbol{n}_1$ follow direct by using Eqs. (2d), (2c) and (3b), respectively. The results are:

$$n_0(r) = \frac{1}{2r} \sum_i \frac{1}{a_i} \int_{|r-a_i|}^{(r+a_i)} r' \rho_i(r') dr' \tag{13a}$$

$$n_1(r) = \frac{1}{2r} \sum_i \int_{|r-a_i|}^{(r+a_i)} r' \rho_i(r') dr' \tag{13b}$$

$$\boldsymbol{n}_1(r) = \frac{1}{4r^2} \hat{\boldsymbol{e}}_r \sum_i \frac{1}{a_i} \int_{|r-a_i|}^{(r+a_i)} r' \rho_i(r') [r^2 + a_i^2 - r'^2] dr'. \tag{13c}$$

Now, the remaining weighted density $n_3(\boldsymbol{r})$ can be obtained by inserting the weight function (2a) into (5). Explicitly, one gets:

$$n_3(r) = \frac{2\pi}{r} \sum_i \int_0^\infty r' \rho_i(r') dr' \int_{|r-r'|}^{r+r'} \Theta(R - a_i) R dR. \tag{14}$$

Notice that the last integral vanishes in the region $|r - r'| > a_i$. When $r > a_i$, this implies that the only non-vanishing contributions come from r' in the region $r - a_i < r' < r + a_i$ (note that the upper integration limit is always greater than a_i

in this case), whereas if $r \leq a_i$ the non-vanishing contributions come from $a_i - r \leq r' < r + a_i$. Moreover, if $r + r' > a_i$, this upper integration limit is to be replaced by a_i. Clearly, this will always happen in region $r > a_i$. Combining these results, we can split the above integral into such distinct regions as follows:

$$n_3(r) = \begin{cases} \dfrac{2\pi}{r} \displaystyle\sum_i \left[\int_0^{a_i - r} r' \rho_i(r') dr' \int_{|r-r'|}^{r+r'} R dR + \int_{a_i - r}^{r + a_i} r' \rho_i(r') \int_{|r-r'|}^{a_i} R dR \right], & r \leq a_i, \\ \dfrac{2\pi}{r} \displaystyle\sum_i \int_{r-a_i}^{r+a_i} r' \rho_i(r') dr' \int_{|r-r'|}^{a_i} R dR, & r \geq a_i. \end{cases} \tag{15}$$

Now, the integrals over R can be readily performed, and the above expressions finally simplify to:

$$n_3(r) = \begin{cases} \dfrac{\pi}{r} \displaystyle\sum_i \left[4r \int_0^{a_i - r} r'^2 \rho_i(r') dr' + \int_{a_i - r}^{r + a_i} r' \rho_i(r') [a_i^2 - (r - r')^2] dr' \right], & r \leq a_i, \\ \dfrac{\pi}{r} \displaystyle\sum_i \int_{r-a_i}^{r+a_i} r' \rho_i(r') [a_i^2 - (r - r')^2] dr', & r \geq a_i. \end{cases} \tag{16}$$

Again, it is important to note that this weight function remains finite at the origin, since the second integral in the first line above has leading term proportional to $\sim r$ in this limit. Notice also that by virtue of the identity in (3a), Eq. (12b) can be obtained from the above equation by making $\boldsymbol{n}_3(r) = -\nabla n_3(r)$.

The expressions provided above show that numerical integration to obtain the weighted densities can be effectively performed considering only one-dimensional integrals over a small region of at most one diameter size around each observation point r. After numerical calculation of the weighted densities, the hard-sphere interaction contribution to the excess chemical potential can be readily computed using:

$$\beta\mu_i(\boldsymbol{r}) = \frac{\delta\beta\mathcal{F}^{hc}}{\delta\rho_i(\boldsymbol{r})} = \sum_\alpha \int \mu_\alpha(\boldsymbol{r}')\frac{\delta n_\alpha(\boldsymbol{r}')}{\delta\rho_i(\boldsymbol{r})}d\boldsymbol{r}', \tag{17}$$

where we have defined $\mu_\alpha(\boldsymbol{r}) \equiv \left.\dfrac{\partial\Phi}{\partial n_\alpha}\right|_{n_\alpha(\boldsymbol{r})}$ as the derivative of the (local) free-energy density in the FMT functional with respect to the weighted ionic densities. Using Eq. (1), the expression above can be simplified to

$$\beta\mu_i(\boldsymbol{r}) = \sum_\alpha \int \beta\mu_\alpha(\boldsymbol{r}')\omega_\alpha^{(i)}(\boldsymbol{r}'-\boldsymbol{r})d\boldsymbol{r}'. \tag{18}$$

In the case of vector weight functions, the above integrals are generalized to a scalar product between the gradient of $\Phi(n_\alpha)$ with respect to the components of the vector density $\boldsymbol{n}_\alpha$ and the corresponding weight density $\boldsymbol{\omega}_\alpha$. Since the vectors $\boldsymbol{\mu}_\alpha(\boldsymbol{r}')$ point in the radial direction $\hat{\boldsymbol{e}}_{r'}$, whereas the weight densities point along the direction of $-\hat{\boldsymbol{e}}_R = (\boldsymbol{r}'-\boldsymbol{r})/R$, these integrals can be written as

$$\int \boldsymbol{\mu}_\alpha(\boldsymbol{r}')\cdot\boldsymbol{\omega}_\alpha^{(i)}(\boldsymbol{r}'-\boldsymbol{r})d\boldsymbol{r}' = \int \frac{|\boldsymbol{\mu}_\alpha(\boldsymbol{r}')|}{R}|\boldsymbol{\omega}_\alpha^{(i)}(R)|\,(r'-r\cos\theta')\,d\boldsymbol{r}', \tag{19}$$

where again $\theta' = \cos^{-1}(\hat{\boldsymbol{e}}_r\cdot\hat{\boldsymbol{e}}_{r'})$ is the angle between the vectors $\boldsymbol{r}$ and $\boldsymbol{r}'$. As before, we can set the z-axis so as to coincide with the observation point direction $\boldsymbol{r}$. The azimuthal integration can thus be trivially performed, while the integration of polar angle can be simplified under the substitution $\cos\theta' = (r^2+r'^2-R^2)/(2rr')$. The above expressions are then simplified to

$$\int \boldsymbol{\mu}_\alpha(\boldsymbol{r}')\cdot\boldsymbol{\omega}_\alpha^{(i)}(\boldsymbol{r}'-\boldsymbol{r})d\boldsymbol{r}' = \frac{\pi}{r^2}\int_0^\infty |\boldsymbol{\mu}_\alpha(r')|r'dr'\int_{|r-r'|}^{r+r'}|\boldsymbol{\omega}_\alpha^{(i)}(R)|\left(r^2+R^2-r'^2\right)dR. \tag{20}$$

Note that, because the weighted densities $n_\alpha(r)$ all possess radial symmetry, the functions μ_α will be also spherical symmetric, as well as the resulting chemical potentials in Eq. (18). As a consequence, all the integrals in each term of this expression can be simplified to a one-dimensional radial integral, $I_\alpha^{(i)}(r)$, whose form is identical

to the corresponding $n_\alpha(r)$ integrals given above, provided the simple replacement $\rho_i(r) \leftrightarrow \mu_\alpha(r)$ is made.

As a final remark we notice that, since the numerical integrals are in practice performed over a finite volume, the upper integration limits over the radial coordinate r' are to be replaced by $R_{min} = min(R_c, r+a_i)$, where R_c is the radius of the confining cell in which integration is performed.

II. FORCE BALANCE ACROSS THE SHELL

We now provide a detailed derivation of the force-balance condition across the spherical charged shell of radius R. Since the system possess spherical symmetry, the net force on an arbitrary point on the shell surface will point in the radial direction. This force can be either positive or negative, resulting in an outward or inward osmotic stress, respectively. The net force on the shell is the force exerted by the surrounding ionic cloud on its surface. On the other hand, the force due to the electrolyte on the shell is the negative of the force that the shell exerts on the ionic system. Due to the spherical symmetry, the force dF acting on each element of area dA on the shell surface is the same. The corresponding pressure is therefore $P = \dfrac{dF}{dA}$. On the other hand, the net force on the wall can be split into electrostatic and hard-sphere contributions. Making use of the spherical symmetry, the electrostatic contribution to the osmotic stress over the surface is

$$\Pi_s^{el} = \frac{1}{A} q \int \varrho_s(\boldsymbol{r})(\boldsymbol{E}_{ion}(\boldsymbol{r}) \cdot \hat{\boldsymbol{e}}_r) d\boldsymbol{r}, \tag{21}$$

where $\varrho_s(r) = Zq\delta(r-R)/4\pi R^2$ is the charge density lying on the shell surface, $\boldsymbol{E}_{ion}$ is the electric field produced by the mobile ions only, $\hat{\boldsymbol{e}}_r$ is the unit vector pointing at the radial direction and $A = 4\pi R^2$ is the surface area. Notice that, while the *net* force on the shell is obviously zero, the radial force on an arbitrary

point on the surface does not vanish. Since the ionic profiles have radial symmetry, application of the Gauss Law allows one to write the ionic electric field as $\boldsymbol{E}_{ion}(r) = Z_{ion}(r)q/\varepsilon r^2\hat{\boldsymbol{e}}_r$, where $Z_{ion}(r)$ is the total ionic charge enclosed within a sphere of radius r. Substituting these results in the above expression provides the following expression for the electrostatic pressure on a given point on the surface:

$$\Pi_s^{el} = \frac{qZE_{ion}(R)}{A} = \frac{ZZ_{in}\lambda_B}{4\pi R^4}, \tag{22}$$

where we have defined $Z_{in} \equiv Z_{ion}(R)$ as the net ionic charge lying *inside* the spherical shell. Since the net ionic charge inside the shell volume has sign opposite to the shell surface charge surface, this contribution to the osmotic stress is usually negative, leading to the shrinkage of the shell surface.

Let us now consider the hard-core ion-wall interaction to the osmotic pressure. According to Newton's third Law, the net radial pressure due to ionic collisions at close contact with the shell membrane can be expressed as

$$\Pi_s^{hs} = \frac{1}{A}\sum_i \int \rho_i(\boldsymbol{r}) \left(\nabla\phi_i^{hs}(\boldsymbol{r}) \cdot \hat{\boldsymbol{e}}_r\right) d\boldsymbol{r}, \tag{23}$$

where $\phi_i^{hs}(\boldsymbol{r})$ is the ion-shell hard-core potential. Using the radial symmetry of both ionic profiles and ion-shell hard-core interactions, the expression above can be conveniently rewritten as

$$\beta\Pi_s^{hs} = -\frac{4\pi}{A}\sum_i \int_0^\infty r^2 \frac{d}{dr}\left(e^{-\beta\phi_i^{hs}(r)}\right)\rho_i(r)e^{\beta\phi_i^{hs}(r)}dr. \tag{24}$$

Note that, in contrast to $\phi_i^{hs}(r)$, the quantity $e^{-\phi_i^{hs}}$ is limited everywhere. This function vanishes at ion-shell overlap, being equal to unity anywhere else. Integration by parts of the above expression yields

$$\beta Pi^{hs} = -\frac{4\pi}{A}\sum_i \left[\int_0^\infty \frac{d}{dr}\left(\rho_i(r)r^2\right)dr - \int_0^\infty e^{-\beta\phi_i^{hs}(r)}\frac{d}{dr}\left(\rho_i(r)r^2 e^{\beta\phi_i^{hs}(r)}\right)dr\right]. \tag{25}$$

Now, noticing that the quantity $\phi_i^{hs}(r)$ vanishes in the regions of non-overlapping, it becomes clear that the integrals above cancel each other in such regions (since $e^{\beta\phi_i^{hs}} = e^{-\beta\phi_i^{hs}} = 1$ there). Moreover, the second integral vanishes when ion and shell overlap. The only contribution left is, therefore,

$$\beta P i^{hs} = -\frac{4\pi}{A}\sum_i \int_{R_-}^{R_+} \frac{d}{dr}\left(\rho_i(r)r^2\right) dr = \frac{4\pi}{A}\sum_i \rho_i(R_-)R_-^2 - \rho_i(R_+)R_+^2, \tag{26}$$

where $R_\pm$ denotes the closest inner/outer ion-shell contact distance. For very thin shells $R_\pm \approx R$. The radial contribution from ion-shell hard-core interactions to the osmotic pressure is then

$$\beta\Pi^{hs} = \sum_i \rho_i(R_-) - \rho_i(R_+). \tag{27}$$

Note that the inner (outer) contact ionic densities dictate the outward (inward) contributions to the osmotic pressure. The overall ionic contribution to the osmotic stress can be obtained by combining of electrostatic and the hard-sphere contributions, Eqs. (22) and (27), respectively,

$$\beta\Pi^{osm} = \sum_i \rho_i(R_-) - \rho_i(R_+) + \frac{ZZ_{in}\lambda_B}{4\pi R^4}. \tag{28}$$

The above expression comprises only *ionic* contributions to the osmotic stress, resulting from corresponding the ion-shell interactions. The *total* osmotic stress should also contain the contribution from the shell electrostatic and elastic self-energies. The electrostatic self-energy is

$$\beta U_s^{self} = \frac{\varepsilon}{8\pi}\int |\boldsymbol{E}_s(\boldsymbol{r})|^2 d\boldsymbol{r}, \tag{29}$$

where $\boldsymbol{E}_s$ stands for the electric field produced by the charged shell. This field vanishes inside the charged shell, while at distances larger than the shell radius it is given by $\boldsymbol{E}_s(\boldsymbol{r}) = Zq/\varepsilon r^2 \hat{\boldsymbol{e}}_r$. Substitution of this expression into the above integral

results in $\beta U_s^{self} = \lambda_B Z^2/2R$. The corresponding contribution to the osmotic stress can be computed from $\beta\Pi = -\dfrac{1}{4\pi R^2}\dfrac{\partial \beta U_s^{self}}{\partial R}$, resulting in

$$\beta\Pi_s^{self} = \frac{\lambda_B Z^2}{8\pi R}. \tag{30}$$

Note that this contribution is always positive. The total electrostatic and hard-sphere contribution to the osmotic stress can finally be written as

$$\beta\Pi_s = \sum_i \rho_i(R_-) - \rho_i(R_+) + \lambda_B \frac{Z(Z+2Z_{in})}{8\pi R^4}. \tag{31}$$