Modelling microgel swelling: Influence of chain finite extensibility

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Microgels exhibit the ability to undergo reversible swelling in response to shifts in environmental factors that include variations in temperature, concentration, and pH. While several models have been put forward to elucidate specific aspects of microgel swelling and its impact on bulk behavior, a consistent theoretical description that chains throughout the microscopic degrees of freedom with suspension properties and deepens into the full implications of swelling remains a challenge yet to be met.

In this work, we extend the mean-field swelling model of microgels from Denton and Tang (J. Chem. Phys. 145, 164901 (2016)) to include the finite extensibility of the polymer chains. The elastic contribution to swelling in the original work is formulated for Gaussian chains. By using the Langevin chain model, we modify this elastic contribution in order to account for finite extensibility effects, which become prominent for microgels containing highly charged polyelectrolytes and short polymer chains. We assess the performance of both elastic models, namely for Gaussian and Langevin chains, comparing against coarse-grained bead-spring simulations of ionic microgels with explicit electrostatic interactions. We examine the applicability scope of the models under variation of parameters such as ionization degree, microgel concentration and salt concentration. The models are also tested against experimental results. This work broadens the applicability of the microgel swelling model towards a more realistic description, which brings advantages when describing suspensions of nanogels and weak-polyelectrolyte micro/nanogels.

I. INTRODUCTION

Microgels are porous, elastic networks of cross-linked polymers spanning the nanometer to micrometer size scale. When immersed in a good solvent, they can reversibly swell in response to changes in environmental conditions, such as changes in temperature, solvent quality, pH and concentration.¹⁻⁴ These soft colloidal particles have gained considerable importance since they confer tunable properties to the suspension, making them highly valuable in several technological applications, such as in drug delivery,⁻⁵⁻⁷ diagnostic,⁸ and cell culture/tissue reconstruction.⁹ The exceptional characteristics of functional microgels primarily arise from their dynamic, permeable, network-like architecture, their flexibility and, most importantly, their capacity to swell in different solvents.³ When swelling or deswelling, microgels either absorb or release solvent, respectively, due to changes in their internal osmotic pressure and interactions, resulting in a size variation of several times their original size.¹⁰ In drug delivery, endogenous stimuli-responsiveness is used to induce microgel swelling and release the cargo as a consequence of the morphological response of the supramolecular assembly.¹¹ Besides, water-swollen networks present various advantages regarding biocompatibility and solubility due to their high hydrophilicity and low interfacial energy,³ as well as storage and transport of guest molecules thanks to their large internal voids.⁵,⁶ Swelling also plays a key role in detection devices since most of the microgel-based sensors rely on their swelling state as sensing mechanism.³ The capability of functionalizing microgel with swelling responsiveness to determined species allows to quantify the concentration of this species, e.g., by means of determination of the volume variation through the reflectance spectrum¹²⁻¹⁴ or by analyzing the effect of swelling on the microgel net charge.¹⁵

In a polar solvent, microgels that incorporate ionic groups through copolymerization can become charged by releasing counterions into the solution. Charge-induced drug binding of drugs to functionalized microgels is a common mechanism for controlled uptake and release in microgel drug delivery.⁵,⁶,¹⁰,¹⁶,¹⁷ To guarantee an efficient loading, the functional microgel should not only possess charged groups but also it should exhibit a net charge that fosters the loading when in contact with the drug buffer.¹⁰ Anionic microgels have proven their potential utilization in the uptake and delivery of, e.g., doxorubicin,¹⁸,¹⁹ ferritin²⁰ among other proteins,²⁰ while cationic microgels for DNA, RNA and oligonucleotides, which results advantageous for gene delivery systems.¹⁰

A deep understanding of the fundamental mechanisms underlying the swelling of ionic microgels and their interaction with other charged species is crucial for further advance in the field. It has been shown that the interplay of electric repulsion among polyelectrolyte chain segments and the osmotic pressure exerted by the counterions can cause a significant expansion in the microgels when contrasted with electrically neutral counterparts.²¹–²³ The presence of salt ions, encompassing those from natural self-dissociation or externally added, increases the population of free co- and counterions, affecting the effective screening of the inherent Coulomb interactions between backbone sites and, consequently, modifying microgel swelling. Furthermore, microgels exhibit a nonzero effective charge that determines the effective microgel-microgel interaction and, hence, the suspension stability, and leads the system to show very interesting phase behavior as compared to usual charged colloidal systems.²³–²⁵

The fast-expanding synthesis field and the ever-expanding array of potential applications require the application of various polymer theories that facilitate the measurement interpretation, helping not only in a fundamental understanding of microgel phenomenology but also supporting their rational design. The addition of new internal degrees of freedom relat-
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fects leads to strong self-repulsion of the backbone charges, motic pressure.

nanogel swelling is governed by screened electrostatic interactions without a relevant contribution by the counterion os-
nanogel swelling behaviors that might be related to demanded suspension properties. A predictive accurate swelling model results then of remarkable importance, when planning on-demand microgel design.

Different theoretical models have been proposed aiming to describe the swelling behavior of microgels. Macroscopic gel models have been used for describing the swelling of microgels suspensions,\textsuperscript{21,26–28} where gel electroneutrality is assumed and the effect of the self-repulsion of the backbone charges on the chain conformation is neglected. Furthermore, these theories are restricted to microgels with relatively uniform charge distributions across the entire network. Scaling and phenomenological models have been proposed and contrasted against coarse-grained simulations for exploring the role of the screened electrostatic interactions between backbone charges upon swelling in nanogels.\textsuperscript{29,30} More sophisticated theories, such as density function theory\textsuperscript{31–33} and variational theory,\textsuperscript{34} have been developed and investigated, to consistently relate microscopic degrees of freedom with microgel swelling. Here the complex coupling between microgel screening, backbone self-repulsion and polymer conformation has been accounted for. Particularly, Denton and Tang have introduced a mean-field cell-model-based framework that links the continuous variations in the counterion density with conformational variation of the polymer and the influence in the microgel electrostatic charge density.\textsuperscript{35} The latter has proven to accurately describe swelling for weakly charged microgels with sizes of a few hundred nanometers. Deepening the understanding of smaller microgels becomes pertinent since this scale of sizes can accentuate features that unfold new potential applications. These new aspects at smaller length scales have been explored. It has been shown that nanogel swelling is governed by screened electrostatic interactions without a relevant contribution by the counterion osmotic pressure.\textsuperscript{29} The reduced screening due to entropic effects leads to strong self-repulsion of the backbone charges, which impacts chain elongation.

In this work, we extend the swelling model introduced by Denton and Tang\textsuperscript{35} for ionic microgel in order to incorporate the finite extensibility effects of the polymer chains. With that, we broaden the applicability scope of the model to include both highly charged and short-chain cases, which gains importance when dealing with nanogels and acid-base charge regulation. Besides, we assess the performance of these swelling methods against coarse-grained MD simulations of a single ionic microgel in a wide range of parameters, as a means to elucidate the accuracy of the theoretical models.

II. THEORY

We model a suspension of ionic microgels as a suspension of ion-permeable soft colloids that is free to exchange microions with a salt reservoir through a semi-permeable membrane. This system can be suitably described in the semi-grand canonical ensemble using cell model approximation,\textsuperscript{35–37} where the semi-grand canonical partition function has the form

\[ \Xi = \Xi_e \Xi_g, \]  

which is given by the product of the electrostatic grand canonical partition function, \( \Xi_e \), and the gel canonical partition function, \( \Xi_g \), for decoupled electrostatic and gel degrees of freedom. The electrostatic grand canonical partition function

\[ \Xi_e(\mu_0, a, R, T) \propto \sum_{N_+ = 0, N_- = 0}^{\infty} \sum_{\beta e, N_+} e^{\beta \mu_0 N_+} \mu_{\beta e}^{N_+} N_+! N_-! \times \]

\[ \times \int_{V_{N_+} + V_{N_-}} e^{-\beta H_e} d\mathbf{r}_1 \ldots d\mathbf{r}_{N_+} d\mathbf{r}_1 \ldots d\mathbf{r}_{N_-} \]

for a system of \( N_+ \) cations and \( N_- \) anions, such that the system is electroneutral when accounting for the charges of the central colloid. The electrostatic component of the Hamiltonian can be decomposed as

\[ H_e = U_m(a) + U_{mu}(\{\mathbf{r}\};a) + U_{\mu\nu}(\{\mathbf{r}\}) \]

\[ = U_m(a) + \sum_{\mu = \pm} \sum_{\nu = \pm} \sum_{r_1} V_{\mu\nu}(\mathbf{r}_1;a) + U_{\mu\nu}(\{\mathbf{r}\}) \]

for \( a \) the microgel radius. Here, \( U_m \) is the microgel electrostatic self energy, \( U_{mu} \) the potential energy due to the interaction between the microgel and the different microionic species, and \( U_{\mu\nu} \) due to microion-microion interactions.

The pressure inside the microgel relative to the bulk osmotic pressure can be defined via a derivative of \( \Omega = -k_B T \ln \Xi = \Omega_e + \Omega_g \) with respect to the microgel volume, \( v = 4\pi a^3/3 \)

\[ \pi = \frac{1}{v} \left( \frac{\partial \Omega}{\partial v} \right)_{\mu_0, R, T} = \pi_e + \pi_g \]

where \( \pi_e \) and \( \pi_g \) correspond to the electrostatic and the gel network contributions. At equilibrium, the pressure inside the microgel should match that one of the bulk, resulting in \( \pi = 0 \). The latter is equivalent to equate the chemical potential of the solvent inside and outside of the microgel, ensuring there is no net transfer of solvent into or out of the gel. This condition leads to a close interconnection between thermodynamic and mechanical equilibrium.\textsuperscript{27}

III. MEAN-FIELD MODEL

In order to provide expressions for the different terms in Eq. (4), we restrict our model to a mean-field approximation, where the microions are modelled as non-interacting charged ideal gasses, neglecting intermicroion correlations. Furthermore, the suspension is described by means of cell model approximation: we consider a single microgel located at the center of a spherical cell, whose radius is determined by the microgel concentration, fulfilling electroneutrality.
Let us consider a single microgel network constituted by a total of $N_{\text{mon}}$ number of monomers, $N_{\text{ch}}$ effective number of chains crosslinked by $N_{\text{cross}}$ tetrafunctional crosslinkers, with $N = N_{\text{mon}}/N_{\text{ch}}$ monomers per chain. Assuming the microgel network to be spherical with swollen equilibrium radius $a$, the linear deformation factor $\alpha$ is given by
\[
\alpha = \frac{a}{a_{\text{coll}}}
\]
with $a_{\text{coll}}$ the dry microgel radius, i.e. the radius of a collapsed (dry) microgel. The latter can be estimated assuming the monomers pack with a volume fraction equal to the one from random close packing.

### A. Electrostatic contribution: Poisson-Boltzmann cell model

Neglecting microion-microion interactions, one can see that the electrostatic contribution is given by\(^{35}\)
\[
\beta \pi_e = -\frac{1}{4\pi a^2} \left[ \frac{\partial \beta U_{\text{int}}(a,b)}{\partial a} + 4\pi \int_0^a \frac{\partial \beta V_{\text{int}}(r,a)}{\partial a} n_{\text{diff}}(r) r^2 dr \right]
\]
with $n_{\text{diff}}(r) = n_+(r) - n_-(r)$, where $n_{\pm}(r)$ are the microion density distributions. For a spherical microgel with the charged sites homogeneously distributed throughout the whole microgel volume, the electrostatic self energy is given by\(^{38}\)
\[
\beta U_{\text{int}}(a) = \frac{3}{5} \beta \pi_0 Z^2,
\]
where $\beta \pi_0$ is the solvent Bjerrum length and $Z$ is the microgel valence. The microgel-microion potential interaction is
\[
\beta V_{\text{int}}(r,a) = \left\{ \begin{array}{ll} \frac{\lambda_0 z_{\mu}}{2} & 0 \leq r \leq a \leq R \\ \frac{\lambda_0 z_{\mu}}{r} & a \leq r \leq R \end{array} \right.
\]
with $z_{\mu} = \pm 1$ for monovalent microions and microgel charge distribution $\rho_{\text{int}}(r) = 3Z\Theta(a-r)/(4\pi a^3)$, with $\Theta(r)$ the step function. Replacing Eqs. (7) and (8) back into Eq. (6), one obtains
\[
\beta \pi_{e,v} = \frac{\lambda_0}{2a} Z \left[ \frac{2}{5} Z - \langle N_+ \rangle + \langle N_- \rangle + \langle r^2 \rangle_+ - \langle r^2 \rangle_- \right]
\]
with $\langle N_{\pm} \rangle = 4\pi \int_0^1 dr r^2 n_{\pm}(r)$ and $\langle r^2 \rangle_\pm = 4\pi \int_0^1 dr r^4 n_{\pm}(r)$. We explicitly compute the microion density profiles from Poisson-Boltzmann (PB) theory. Assuming the cell to be in osmotic equilibrium with a microion reservoir of concentration $2n_{\text{res}}$, and considering Boltzmann distribution for the microions densities, $n_{\pm}(r) = n_{\text{res}} e^{\Phi(r)}$, with $\Phi(r) = \beta e \psi(r)$ the reduced system electric potential, the Poisson equation is given by
\[
\Phi''(r) + \frac{2}{r} \Phi'(r) = \left\{ \begin{array}{ll} \kappa^2 \sinh[\Phi(r)] - \frac{3Z\lambda_0}{a^2} & 0 \leq r \leq a \\ \kappa^2 \sinh[\Phi(r)] & a < r \end{array} \right.
\]
with $\kappa^2 = 8\pi\lambda_B n_{\text{res}}$, and boundary conditions
\[
\Phi(0) = 0 \quad \text{and} \quad \Phi'(R) = 0
\]
for a microgel with negatively backbone charges and monovalent microions. This quantity is relevant because it is deeply related to the electrostatic osmotic pressure in the microgel. Besides, it is also connected to the suspension stability\(^{39,40}\) via determining the effective microgel-microion interaction\(^{41}\).

### B. Gel contribution

The gel contribution for a homogeneously charged microgel, formed by a total of $N_{\text{mon}} = N_{\text{ch}} \times N + N_{\text{cross}}$, monomers in the network arranged in chains $N_{\text{ch}}$ of $N$ monomers each linked by $N_{\text{cross}}$ tetrafunctional crosslinkers, is
\[
\pi_\text{gel} = \pi_0 + \pi_{\text{elas}}
\]
where
\[
\beta \pi_0 = -N_{\text{mon}} \left[ \alpha^3 \ln(1 - \alpha^{-3}) + \chi \alpha^{-3} + 1 \right]
\]
includes mixing entropy contribution from solvent and monomers and solvent-polymer interaction contribution, characterized by the Flory $\chi$ parameter; and $\pi_{\text{elas}}$ is the elastic network contribution. The latter is given by
\[
\beta \pi_{\text{elas}} = -\frac{N_{\text{mon}}}{N} \left( \frac{R_e}{R_0} \right)^2 = -N_{\text{mon}} \left( \frac{R_e}{bN} \right)^2
\]
for simple Gaussian chains disregarding crosslinkers, with $R_e$ the single chain end-to-end distance. $R_0 = l b N^*$ is the end-to-end distance of a free chain in solution, with $b$ is the mean monomer-monomer distance, while $l$ and $v$ are dimensionless quantities that depend on the chosen chain model.\(^{26,42,43}\) In our case, we have taken $l = 1$ and $v = 1/2$ for ideal chains. Alternatively,
\[
\beta \pi_{\text{elas}} = -\frac{N_{\text{mon}}}{3R_{\text{max}}} \left( \frac{R_e}{R_{\text{max}}} \right)
\]
which corresponds to the Langevin chain model that accounts for finite extensibility of the chains. Here, $R_{\text{max}} = bN$ is the chain contour length.\(^{42-44}\) For practical implementation, we
ne to express Eqs. (15) and (16) in terms of the linear deformation factor $\alpha$, and to establish a relationship between $R_e$ and both the gel volume $v$ and $\alpha$. For a diamond-lattice unit cell with lattice parameter $a_d$, 16 chains produce a total volume $V = a_d^3$. Then, the total volume of a network is approximately $V_{\text{gel}} = N_{\text{ch}} V_{\text{ch}} = N_{\text{ch}} a_d^3 / 16$, where $V_{\text{ch}}$ is the swelling volume yield by a single chain. Assuming that the distance between the nearest-neighbor crosslinkers is equal to the end-to-end chain distance $R_e$, we see that $R_e = \sqrt{3} a_d / 4$, then

$$a_d = \frac{4 R_e}{\sqrt{3}}$$

Therefore, the total volume of the network as function of $R_e$ can be approximated as

$$V_{\text{gel}} = \frac{4}{3\sqrt{3}} N_{\text{ch}} R_e^3.$$  

Furthermore, we can see that

$$\frac{R_e}{bN} = 3^{1/6} \frac{a_{\text{coll}}}{bN} \sqrt{N_{\text{ch}}} \alpha = A \alpha$$

with

$$A = 3^{1/6} \frac{a_{\text{coll}}}{bN} \sqrt{N_{\text{ch}}}$$

where we have used $V_{\text{max}} = 4 N_{\text{ch}} (bN)^3 / (3\sqrt{3})$ and $V_{\text{coll}} = 4 \pi a_{\text{coll}}^3 / 3$. Remember that $a_{\text{coll}}$ is obtained from the total number of monomers, assuming that it is the radius of a sphere with all monomer collapsed according to a volume fraction equal to $\phi_{\text{coll}} = \phi_{\text{rep}}$.

Replacing back, we obtain

$$\beta \pi_{\text{elas}} v = N_{\text{mon}} (A \alpha)^2$$

for Gaussian chains, and

$$\beta \pi_{\text{elas}} v = -\frac{N_{\text{mon}}}{3} A \alpha \xi^{-1} (A \alpha)$$

for Langevin chains. Notice that by Taylor-expanding the right-hand side of last equation around $\alpha = 0$, Gaussian expression in Eq. (21) is recovered at first order.

In Fig. 1, we plot a representative case of the gel pressure contribution $\pi_g$ with both Gaussian (blue continuous line) and Langevin (red continuous line) models for different swelling ratios $\alpha$. The common contribution $\pi_0$ from Eq. (14) is depicted with dashed gray line, while the elastic contributions $\pi_{\text{elas}}$ for Gaussian, Eq. (21), and Langevin, Eq. (22), models are depicted in dashed blue and dashed red lines, respectively. We observe that both models present similar behavior at small $\alpha$: For $\alpha \to 1$, namely $\alpha \to a_0$, the gel osmotic pressure diverges, while it is monotonically increasing with increasing $\alpha$. For $\alpha$ such that $R_e \to R_{\text{max}}$, $\pi_{\text{elas}}$ for the Langevin model diverges since the chains approach their maximum elongation. Notice that for $\alpha$ such that $\beta \pi_g = 0$, we obtain the equilibrium microgel size for neutral case, with Gaussian model predicting larger equilibrium size than the Langevin case. We also see that the total gel pressure $\pi_g$ is dominated by $\pi_0$ contribution for $\alpha \approx 1$, and by $\pi_{\text{elas}}$ otherwise. This holds particularly for short chains, with $N$ in the order of tens of monomers. With increasing $N$, $|\pi_{\text{elas}}|$ decreases, with $\pi_0$ becoming the dominant contribution in the limit $N \to \infty$ (see Fig. S1). Moreover, in this limit, the elastic contribution from Langevin model tends to the contribution from Gaussian model $\pi_{\text{elas}, L} \to \pi_{\text{elas}, G}$, as seen in the inset of Fig. 1.

IV. SIMULATION MODEL

Our coarse-grained simulation model of microgels is based on the cell-model picture used in the theoretical model. We simulate a single microgel in a cubic simulation box, whose size is determined by the system microgel concentration. Differently from the theoretical case, we use a cubic cell, with periodic boundary conditions. This model resembles the theoretical picture for low concentrations, for which microgel double layer does not interact with its image, $\kappa^{-1} \ll L$, with $L$ the simulation box length. A single microgel network is created by linking several straightened polymer chains of $N$ monomers per chain in spherical fashion according to a diamond lattice arrangement, as exemplified in Fig. 2(a). The resulting microgel contains $N_{\text{ch}}$ chains linked by $N_{\text{cross}}$ crosslinkers. The polymer chains and the crosslinkers are represented using the bead-spring Kremer-Grest model, where the beads interact via the Weeks-Chandler-Andersen (WCA) potential and are linked with FENE bonds. The WCA potential has the form

$$V_{\text{WCA}}(r) = \begin{cases} 4 \epsilon \left[ \left( \frac{\sigma}{r} \right)^{12} - \left( \frac{\sigma}{r} \right)^{6} + \frac{1}{4} \right], & r \leq r_c \\ 0, & r > r_c \end{cases}$$

Figure 1. Reduced gel pressure contributions versus trial swelling ratio $\alpha_{\text{trial}}$ for both elastic models for $N = 20$. Inset: Reduced elastic pressure contribution $\pi_{\text{elas}}$ versus $\pi_{\text{elas}, G}$ for $N = 20, 200, 2000$. Other system parameters: $N_{\text{ch}} = 80, N_{\text{cross}} = 75, \chi = 0.5, \sigma = 0.355 \text{ nm}$. https://orcid.org/0000-0001-5548-7889 License: CC BY 4.0
with \( r_c = 2^{1/6} \sigma \). Here \( \sigma \) is taken as unit of distance and \( \varepsilon \) is taken as unit of energy. For the FENE bonds,

\[
V_{\text{bond}}(r) = \frac{1}{2} k_{\text{bond}} r_c^2 \log \left[ 1 - \left( \frac{r}{r_c} \right)^2 \right] \tag{24}
\]

with stiffness \( k_{\text{bond}} = 30 \varepsilon / \sigma^2 \) and divergence length \( r_c = 1.5 \sigma^{4/7} \). Salt and counterions are also modeled by WCA interacting beads and the solvent is modeled implicitly. Electrostatic interactions are accounted explicitly by adding the corresponding Coulomb interaction to the charged particles. In the system, we find anionic polymer beads, the cationic released counterions and ion monovalent ion pair from the salt, such the system electroneutrality is preserved.

The system evolution is governed by Langevin dynamics according to

\[
m_i \dot{v}_i = f_i - \gamma v_i + \sqrt{2 \gamma k_B T} w
\]

for every particle \( i \), with \( m_i \) the particle mass, \( \gamma \) friction constant, \( x_i \) the positions and \( v_i \) the velocities. The conservative force \( f_i \) results from the interparticle interaction, and the stochastic force \( w \) fulfills \( \langle w \rangle = 0 \) and \( \langle w_i(t) w_j(t') \rangle = \delta_{ij} \delta(t-t') \). The mass of all particles is taken equal to the unity and the electrostatic interactions are calculated via the P3M method.\(^{48}\)

For given topology, namely fixed \( N_{\text{ch}} \) and \( N_{\text{cross}} \), various chain lengths \( N \) have been explored as well as different system parameters and microgel backbone charge. The simulation is initialized with a favorable microgel configuration of an equivalent neutral case, and we let the system evolve until reaching steady state (see Fig. 2b). Later, we measure the network radius of gyration and density distributions for characterizing the suspension and the microgel swelling.

Simulations are performed utilizing the simulation package ESPResSo.\(^{49,50}\)

V. RESULTS

We assess the theoretical models of ionic microgel swelling, for both elastic formulations, by contrasting them against coarse-grained implicit-solvent simulations. In this regard, the parameters have been chosen such that the most relevant conditions are explored and analyzed. For that, the following parameters have been examined. For microgel topology, we have taken two cases: 1- \( N_{\text{ch}} = 148 \) and \( N_{\text{cross}} = 99 \); and \( N_{\text{ch}} = 136 \) and \( N_{\text{cross}} = 87 \). We have also considered microgel concentrations such that the monomer concentration varies in the range \( c_{\text{mon}} = 1 \times 10^{-5} - 0.03 \sigma^{-3} \); ionization degrees in the range \( Z/Z_{\text{max}} = 0 - 1 \); system salt concentrations in the range \( c_{\text{sys}} = 0 - 10 \) mM; and \( \chi = 0.1 \). We numerically solve the nonlinear PB equation using the MATLAB routine bvp4c.\(^{51}\)

A. Swelling modelling in the salt-free limit

In order to understand swelling predictions from the different models, we primarily focus on the salt-free limit, where the microgel swelling is most pronounced. Firstly, we consider the swelling of an instructive case and analyze how the equilibrium size depends on the different osmotic pressure contributions. In Fig. 3a, we observe the electrostatic pressure contribution \( \pi_e \) and the gel contributions \( \pi_g \) for Gaussian and Langevin model versus trial swelling ratio \( \alpha_{\text{trial}} = a_{\text{trial}}/a_0 \). As observed, \( \pi_e \) is positive and decreases for increasing \( \alpha_{\text{trial}} \), and increases with growing microgel bear charge at constant swelling \( \alpha_{\text{trial}} \). Namely, it mainly contributes to a microgel expansion. This contribution is counteracted by \( \pi_g \), which is smaller that zero for swelling larger that the equilibrium size for neutral case. Recall that the equilibrium microgel swelling is given at the swelling ratio such that \( \pi_e + \pi_g = 0 \). From the figure, we see that the slow monotonous increase of \( \pi_g \) for Gaussian model (continuous blue line) with growing...
swelling ratio leads to a pronounced increase of the equilibrium size as we rise the microgel bare charge. On the other hand, \( \pi_e \) in the Langevin model (dashed red line) diverges for the swelling ratio corresponding to the maximum extension of the chains, indicated in the figure with a vertical dashed gray line, which causes a saturation of the equilibrium size as we increase microgel bare charge. In Fig. 3b, we plot the equilibrium swelling ratio relative to the dry radius (linear deformation factor) versus bare charge \( Z \) for both elastic models. We see that the Gaussian model presents a steeper growth than the Langevin case when increasing \( Z \). With further increase in \( Z \), the chains reach their maximum extension and Langevin equilibrium size saturates, while Gaussian equilibrium size remains growing largely overcoming Langevin one.

![Figure 3](image_url)

Figure 3. (a) Normalized electrostatic osmotic pressure \( \pi_e \) and gel osmotic pressure \( \pi_g \) versus trial swelling ratio \( \alpha_{\text{trial}} \) for different elastic models and various microgel bare valence \( Z \): (b) equilibrium swelling ratio, \( \alpha_{\text{eq}} \) versus bare microgel valence \( Z \) for different elastic models. Points correspond to the cases in (a). Other system parameters: \( \lambda_t = 0.71 \text{ nm}, c_{\text{res}} = 100 \mu \text{M}, \phi_0 = 1.1e - 5 \). Further parameters similar to Fig. 1.

In order to test both models, we compare their swelling predictions versus coarse-grained microgel simulations. One important point to take into account when comparing against simulations and experiments is the choice of the reference microgel volume. The description of swelling is formulated in terms of the (collapsed) dry microgel volume, which is, however, very difficult to access experimentally nor in coarse-grained simulations. After extensive drying, a real gel network might still contain a significant amount of solvent, while it is impossible to define a dry state in simulations with implicit solvent and soft interactions.\(^{42,43}\) Therefore, when contrasting versus simulations, we are going to use the reference collapsed volume as a fitting parameter in the theoretical models.

Figure 4a shows the microgel equilibrium swelling ratio versus ionization degree for microgels formed by chains of different number of monomers \( N \) at constant \( N_{\text{cross}} \) and \( N_{\text{ch}} \). Here, the swelling ration is determined via the microgel radius of gyration \( R_g \) relative to the radius of gyration from the corresponding neutral case \( R_g(Z=0) \). We observe how the swelling ratio increases when increasing the ionization degree \( \zeta = Z/Z_{\text{max}} \) at constant \( N \), with \( Z_{\text{max}} \) being the charge for which each monomer in the network holds a monovalent charge of \(-e\). Simulations of short-chain microgels depict a mild swelling for growing ionization degree, but flattening at large ionizations. The fact that the chains are short eases configurations with end-to-end distance closer to their contour length \( R_{\text{max}} \). As \( N \) is enlarged, the swelling becomes more pronounced at low ionization with a likewise flattening for larger ionizations. We also notice that the microgel size increases with increasing \( N \) at constant ionization degree as expected. One can see that microgel \( R_g \propto N^\delta \) with \( \delta = 0.57 \pm 0.01 \) for the neutral case, which is close to the expected \( v = 0.6 \) for self-avoiding chains; while, \( \delta = 0.94 \pm 0.01 \) for \( \zeta = 0.5 \), as seen in Fig. S3a, close the expected \( \delta = 1 \) from scaling theory.\(^{44}\)

The corresponding theoretical predictions are plotted with continuous lines for the Gaussian model and dashed lines for the Langevin model, which are calculated considering a reference collapsed volume such that the monomers in the microgel are arranged occupying a volume fraction of \( \phi_{\text{coll}} = 0.22 \) for all \( N_{\text{ch}}'s \). For the shortest chains, \( N = 10 \), the mild swelling is well approximated by the Langevin model and overestimated by the Gaussian one at large \( \zeta \). With increase of \( \zeta \), we observe that both models tend to underestimate the steep swelling at low \( \zeta \) with a more pronounced effect at larger \( N \). At large \( \zeta \), the Gaussian model tends to strongly overestimate swelling, while the Langevin approximately captures the flattening. We see then that Langevin model more accurately describes the swelling ratio in the whole range of charges for a wide variation on chain length.

Another relevant quantity that is closely related to the electrostatic osmotic pressure and the microgel swelling is the microgel net charge \( Z_{\text{net}} \), presented in Eq. (12). In Fig. 4b, we observe how \( Z_{\text{net}} \) varies with increasing \( \zeta \) for different \( N \) for simulations and theory. In simulations, \( Z_{\text{net}} \) is determined by counting the number of counterions inside the spherical microgel, where the equilibrium radius \( a_{\text{eq}} \) is determined from the polymer density profile \( P_{\text{pol}}(r) \) such that \( P_{\text{pol}}(a_{\text{eq}}) = 0.01 \). This criterion corresponds to the abrupt decrease of the density profile, which approximately delimits the smooth microgel edge and nearly corresponds to radii where the density profiles of the released counterions present a change in behavior, in case of ionic microgels (see Fig. S2). At constant
swelling ratio $\frac{R}{R_0}(Z = 0)$ net charge $\zeta$

Figure 4. (a) Swelling ratio $R_g/R_g(Z = 0)$ and (b) microgel net charge $Z_{\text{net}}$ versus ionization degree for salt-free system for various $N$. Points correspond to simulations, continuous lines correspond to Gaussian chains and dashed lines to Langevin chains. System parameters: $\rho = 5\text{e}^{-5}, N_{\text{ch}} = 148, N_{\text{cross}} = 99, \chi = 0.1, a_0$ such that monomer concentration in gel is $\phi_{\text{coll}} = 0.22 N = 10, 20, 40, 60; N_{\text{mon}} = 1480, 2960, 5920, 8880; L = 316, 394, 494, 564$.

From the simulations, we see that $|Z_{\text{net}}|$ increases with increasing $\zeta$, but rapidly saturates, indicating a large retention of counterions in the microgel interior due to the electrostatic interactions. The large fluctuations of $Z_{\text{net}}$ at large $\zeta$ and the mild decrease for both large $\zeta$ and small $N$ are due to fluctuations in the estimation of $\sigma_{\text{eq}}$, as seen in Fig. S4a. The latter occurs because of the error present in the density profiles for highly swollen microgels.

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From the theories, a slightly different behavior of $Z_{\text{net}}$ is predicted. Both theories describe the increase of $|Z_{\text{net}}|$ with increasing $\zeta$ with a larger prediction of $|Z_{\text{net}}|$ from Gaussian model. However, the saturation that is observed in simulations is not present in the theoretical cases. In order to understand such discrepancies, we have calculated $Z_{\text{net}}$ from PB theory, but accounting for the microgel sizes obtained from the simulations. These results are shown in Fig.S4(a) for fitting factor $\phi_{\text{coll}} = 0.22$, which produces the best fitting of the swelling ratio $R_g/R_g(Z = 0)$, and in Fig.S4(b) for fitting factor $\phi_{\text{coll}} = 0.05$, which produces the best fittings of the absolute microgel sizes $a_{\text{eq}}$. The figures show that accounting for the correct microgel size from the simulations in PB theory does not correctly reproduce $Z_{\text{net}}$ behavior at large $\zeta$ either. We observe indeed that the qualitative shape of the swelling models and the PB theory with the correct sizes are alike, with the clear overestimation of $|Z_{\text{net}}|$ at large microgel sizes. That allows us to infer that the discrepancies lay on the differences in spatial charge densities between the theoretical models and the simulation model, and on the treatment of the correlations. Differently from the assumed homogeneous charge distribution of the theoretical PB framework, the chain-like arrangement of the charges in the simulation model favors Manning condensation for ionization degrees $\zeta \geq 0.5$, since we take $\lambda_B = 2\sigma$. The strong counterion condensation leads to a larger presence of counterions inside the microgel, diminishing $|Z_{\text{net}}|$ and augmenting the screening inside the microgel, which results in a weaker swelling. This explains the strong overestimation of $|Z_{\text{net}}|$ as well as the tendency to an overestimation of the microgel size at large ionization degrees by the theoretical models. Moreover, the saturation of $Z_{\text{net}}$ agrees with the fact that Manning condensation induces a condensation of ions such that the Manning parameter $\Gamma = 1$, leading to a similar effective network charge density for $\zeta > 0.5$. In conclusion, the slow growth in swelling ratio at large ionization degrees is strongly influenced not only by the finite extensibility of the polymer chains, but also by Manning condensation, specially at large $N$.

So far we have fit $\phi_{\text{coll}}$ using same value for all $N$'s for both methods. An alternative option would be trying with a different value of $\phi_{\text{coll}}$ for the Gaussian case. But the model is not able to resemble the saturation in swelling. The systematic deviations of the theoretical models at low and large $\zeta$ can be then attributed to the strong counterion-polymer correlations induced by the chain-like structure of the network, with minor influence of the disregard for polymer and ion excluded volumes as well as ion correlations in the mean-field approach. The presence of excluded-volume effects in simulations lead into a stronger swelling due to larger end-to-end distances of the polymer chains because of the excluded volume of the monomers and a reduction in the screening inside the microgel because of ion correlations. This results in the steeper swelling at low $\zeta$. In the theoretical model, the differences with the simulations can be bypassed by fine tuning $\phi_{\text{coll}}$ for low and high $\zeta$, in particular with Langevin model.

Another interesting feature of ionic microgels is the microgel deswelling with increasing microgel concentration, for dilute suspensions. This effect is explored in simulations by changing simulation box size. In Fig. 5, we observe how the swelling ratio relative to microgel size at the dilutest concentration varies by increasing microgel concentration for different ionization degrees. Notice that the curves are vertically shifted by 0.5 units for better visualization. In our context, microgel concentration is equivalent to the monomer concentration for fixed microgel structure. From the simulations (points), we observe that the swelling ratio decreases very slowly at small concentrations and presents a
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Figure 5. Swelling ratio $R_g/R_g(L = 800)$ versus monomer concentration $N_{\text{mon}}/L^3$ for salt free system for the indicated ionization degrees $\zeta$. Points correspond to simulations, continuous lines correspond to Gaussian chains and dashed lines to Langevin chains. The different ionization cases are shifted vertically by +0.3 for better visualization. System parameters: $N_{\text{ch}} = 136$, $N_{\text{cross}} = 87$, $\chi = 0.1$, $a_0$ such that monomer concentration in gel is $\phi = 0.22 N = 40$; $N_{\text{mon}} = 5440$; $L = 800$, \ldots 60.

Figure 6. Swelling ratio $R_g/R_g(c_{\text{salt}} = 0)$ versus system salt concentration for the indicated ionization degrees $\zeta$. Points correspond to simulations, continuous lines correspond to Gaussian chains and dashed lines to Langevin chains. System parameters: $N_{\text{ch}} = 148$, $N_{\text{cross}} = 99$, $\chi = 0.1$, $a_0$ such that monomer concentration in gel is $\phi = 0.22 N = 40$; $N_{\text{mon}} = 5920$; $L = 494$.

more pronounced decrease at larger ones for fixed ionization. These deswelling is a consequence of the increased screening inside the microgel due to the (entropy-mediated) migration of counterions into the microgel because of the effective reduction of bulk volume resulting from the larger microgel concentration.\textsuperscript{15,22,35,53} The latter is endorsed by the decrease in $|Z_{\text{gel}}|$ with augmenting microgel concentration, see Fig. S5. When comparing different ionizations, microgels deswell with approximately same rate at low concentrations independently of ionization degree. While at high concentrations, microgels with larger ionization degree tend to deswell faster, because the increase in inner screening is more pronounced due to the larger system ionic strength, namely the presence of more counterions in the system.

Analyzing the theoretical predictions, we observe that both methods perform fairly well, especially at high ionizations as expected. Similarly to Fig. 4, we have taken $\phi_{\text{coll}} = 0.22$. Both models describe qualitatively well the deswelling as microgel concentration is increased. However, they present an overestimation of swelling a large concentrations, which is more significant in the Gaussian case. The weaker performance of the methods at low ionization degrees is related to a stronger migration of counterions into the microgel, as seen in the steepest decrease in the microgel net charge, see Fig. S5.

B. Swelling for salt variation

So far we have considered the salt-free case, where no extra screening is present but just the one from the released counterions and, therefore, the electrostatic interactions are the strongest. Despite its theoretical interest, this is a rather instructive case and of limited application. Although experimentally it is possible to reproduce to a well approximation the salt-free limit by means of, for instance, ion-exchange resines,\textsuperscript{52,53–55} in most of the cases extra ions from salt dissociation are present. Moreover, the role of the extra added salt results fundamental for biomedical and drug-delivery applications. Therefore, we explore next the effect of salt in swelling and the performance of the methods under these conditions.

In the simulations, we vary the system salt concentration by adding extra monovalent ion pairs to the system and analyze how the microgel swelling changes. In Fig. 6, we observe microgel swelling relative to the salt-free size versus system salt concentration for the indicated ionization degrees at constant microgel concentration. Notice that the data is vertically shift by 0.1 units for the different ionization degrees to favor a better visualization. For the three cases, we observe a similar decrease of the microgel swelling ratio as salt concentration increases as it is expected from experiments.\textsuperscript{15}

When comparing against the theoretical models, we first must notice that the theory is formulated within a semi-grand canonical ensemble, with the system open for microions in contact with a microion reservoir of fixed concentration. Due to the Donnan potential, the system salt concentration $n_{\text{sys}} \leq n_{\text{col}}$ depending on the different species concentration. Notice that the Donnan potential hinges on microgel swelling. Therefore, the system salt concentration is determined within the theory from the coion concentration at equilibrium swelling, see Fig. S6. Figure 6 shows that both theoretical models agree with the simulations qualitatively, with an overestimation of the microgel size at low ionization similar to the observations in Figs. 4 and 5. On contrary to earlier cases, Langevin model is generally larger than the Gaussian one, which leads to a closer agreement between the Gaussian model and the simulations.
C. Comparison with experiments

Finally, we compare the performance of the methods against experimental measurements of microgel size for varying microgel concentration, for weakly-crosslinked ionic microgels in the salt-free limit. The system consists of loosely cross-linked poly(N-isopropylacrylamide-co-acrylic acid) (PNIPAM-co-PAA) microgels dispersed in deionized water at room temperature, neutral pH and various microgel concentrations \( c_{\text{mic}} \). We assume a salt-free solution since the samples were flame-sealed together with an ion exchange resin, which hinders the presence of additional salt ions. We assume that every microgel possesses a valence \( Z_{\text{max}} = 3.7 \times 10^4 \), which has been measured combining conductivity titration and light scattering. We have considered \( N_{\text{mon}} = 3 \times 10^6 \) following Refs. \(^{34,35} \), \( \sigma = 0.7 \) for NIPAM monomers \(^{36} \) and \( \phi_{\text{coll}} = \phi_{\text{cap}} \approx 0.64 \), resulting in \( a_0 = 83.68 \text{ nm} \). Taking \( x = N_{\text{ch}}/N_{\text{mon}} \) and \( \chi \) as fitting parameters, we fit experimental measurements with the presented theoretical models. The experimental results are depicted in Fig. 7 using points. Here, we plot the swelling ratio given by the microgel radius \( a \) over a reference microgel radius \( a_{\text{ref}} \), which is measured at the smallest experimental concentration \( c_{\text{mic}} = 0.0167 \mu \text{M} \). We observe that the swelling steeply decreases with increasing \( c_{\text{mic}} \), tending to flatten at large concentrations. This behavior is similar to that in Fig. 5 (presented in semilog scale). Fitted theoretical predictions for \( \chi = 0.5 \) and \( x = 0.001 \) are plotted with continuous lines. Predictions from the different elastic models are indistinguishable in the presented scale. We see that both models accurately capture the microgel shrinking at low concentrations, while they qualitatively capture swelling flattening at large concentrations slightly underestimated microgel size. Fitting parameters agree with those obtained in Ref. \(^{22,53} \), where a variation of the Gaussian model presented in Eq. (15) has been used for describing then elastic pressure contribution. In Ref. \(^{34} \), the effect of crosslinking is accounted for, while we have drop this contribution in order to agree with Langbein model in the limit of small deformation. Incorporation of this contribution leads typically to slightly smaller microgel size predictions, with marginal influence in the swelling ratio behavior.

In the inset of Fig. 7, we plot the model-predicted microgel net charge versus \( c_{\text{mic}} \), which decreases with increasing concentration as expected. From static light scattering experiments, the experimental net charge for the swollen microgels is \( |Z_{\text{net}}| \approx 300^{22,23} \) which is 2 orders of magnitude smaller than \( Z_{\text{max}} \). On the other hand, the averaged \( Z_{\text{net}} \) from theory is one order of magnitude smaller than the experimental \( Z_{\text{max}} \), which qualitatively agrees with the trend of the experiments and proves the net charging of microscopic networks and the heterogeneous distribution of microions between inside and outside of the counterions. The quantitative difference in \( Z_{\text{net}} \) is in agreement with the overestimation of \( Z_{\text{net}} \) already observed in the simulations. We notice then that the approximate nature of both coarse-grained models, namely electrostatic and gel parts, lead observables to acquire values that may differ from the experimental ones, but maintaining overall consistency and qualitative agreement with further system observables and parameters.

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Figure 7. Equilibrium microgel radius versus microgel concentration for PNIPAM-co-PAA microgels. Points corresponds to experimental results \(^{22,53} \) and lines to theory, where differences between Gaussian and Langevin chains are indistinguishable. Microgels consist of \( N_{\text{mon}} = 3 \times 10^6 \) monomers with titration valence \( Z = 3.5 \times 10^4 \) in dionized water \((c_{\text{res}} \to 0) \) at \( T = 293.15 \text{ K} \). Furthermore, \( \sigma = 0.7 \) for NIPAM monomers \(^{36} \) and \( \phi_{\text{coll}} = \phi_{\text{cap}} \approx 0.64 \), with \( a_0 = 83.68 \text{ nm} \). The fitting parameters are \( \chi = 0.5 \) and \( x = N_{\text{ch}}/N_{\text{mon}} = 0.001 \).

VI. CONCLUSIONS

In this work, we have introduced a variation of the theoretical mean-field model from Denton and Tang \(^{35} \) for describing swelling of ionic microgels, which improves and extends its application in a wide range of the parametric space. Denton-Tang model \(^{35} \) combines Poisson-Boltzmann theory for describing electrostatics with Flory-Rehner theory for the polymer properties in order to provide expressions of the microgel osmotic pressure, which is used to determine the microgel equilibrium size. We have incorporated the finite extensibility of the polymer chains in the model by replacing the expression of elastic energy contribution of Gaussian chains by the one from the Langevin model. The later allows to describe the polymer chains with finite extensibility by properly accounting for the effect of the stretching forces in the estimation of the chain end-to-end distance.

We have assessed both models, namely the original model for Gaussian chains and the modified one for Langevin chains, through implicit-solvent coarse-grained simulations in a wide range of microgel concentrations, ionization degrees and salt concentrations. The simulations consisted of a single diamond-lattice microgel in a simulation box whose size was determined by the suspension concentration. The microgel was constructed using Kremer-Grest bead-spring model for the polymer and restrictive primitive model for the electrostatic interactions. Its time evolution was computed using MD with Langevin thermostat.

By varying different system parameters, we have observed that both models perform with same accuracy when descri-
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swelling for low ionization degrees, dilute microgel concentrations and low salt concentrations. For middle and high ionization degrees and high microgel concentrations, utilization of Langevin model remarkably improves swelling predictions.

When varying system salt concentration, both swelling models perform similarly well at larger ionization degrees as compared to the simulations. While Gaussian elastic model turns out to be slightly better than the Langevin one at the lowest ionization.

Furthermore, we see that both swelling models accurately describe swelling of weakly crosslinked PNIPAM-co-PAA microgels, when varying microgel concentration. Comparison against experiments for microgels with typical size of a few hundreds of nanometers shows that both elastic models predict approximately similar swelling with almost indistinguishable estimations, in accordance with the limiting behavior of Langevin model for large polymerisation degree, \( N \gg 1 \).

The models also provide other relevant quantities for microgel characterization such as the microgel net charge \( Z_{\text{net}} \), which is related to the microgel-microgel effective interaction and, therefore, to the suspension structure and stability; and the micron size density profiles, related to the microgel loading by ionic species. By looking at \( Z_{\text{net}} \), one observes that the theoretical swelling models strongly overestimate the simulation net charge, suggesting a strong influence of Manning condensation effects in the microgel swelling due to the chain-like charge distributions of the microgel network.

Overall, the incorporation of finite extensibility in the microgel swelling model improves swelling description in the short-chain and large-deformation limits and for high ionization degrees, enhancing the accuracy of the swelling model in this region of the parameter space. This aspect becomes relevant when studying both suspensions of nanogels and swelling of microgels made of weak polyelectrolytes, where ionization degree and microgel swelling are deeply coupled.

With the current study, we aim to contribute with a theoretical model that provides a description closer to realistic microgels, and that allows for an efficient systematic study of microgels swelling properties.

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DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

SUPPORTING INFORMATION

Figures S1-S7.

CONFLICT OF INTEREST STATEMENT

The authors have no conflicts to disclose.

AUTHOR CONTRIBUTIONS

**Mariano E. Brito:** Conceptualization (lead); data curation; formal analysis; methodology; investigation; software; validation; visualization (lead); writing – original draft ; writing – review & editing. **Christian Holm:** Conceptualization (supporting); formal analysis; funding acquisition; investigation; project administration; resources; supervision; visualization (supporting); writing – review & editing.

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