

## Swelling of particle-encapsulating random manifolds

Emir Haleva and Haim Diamant\*

*School of Chemistry, Raymond & Beverly Sackler Faculty of Exact Sciences, Tel Aviv University, Tel Aviv 69978, Israel*

(Received 20 June 2008; published 22 August 2008)

We study the statistical mechanics of a closed random manifold of fixed area and fluctuating volume, encapsulating a fixed number of noninteracting particles. Scaling analysis yields a unified description of such swollen manifolds, according to which the mean volume gradually increases with particle number, following a single scaling law. This is markedly different from the swelling under fixed pressure difference, where certain models exhibit criticality. We thereby indicate when the swelling due to encapsulated particles is thermodynamically inequivalent to that caused by fixed pressure. The general predictions are supported by Monte Carlo simulations of two particle-encapsulating model systems: a two-dimensional self-avoiding ring and a three-dimensional self-avoiding fluid vesicle. In the former the particle-induced swelling is thermodynamically equivalent to the pressure-induced one, whereas in the latter it is not.

DOI: [10.1103/PhysRevE.78.021132](https://doi.org/10.1103/PhysRevE.78.021132)

PACS number(s): 64.60.De, 87.16.D-, 64.60.Cn, 68.35.Md

## I. INTRODUCTION

There has been considerable interest in the past few decades in the statistical mechanics of membranes and surfaces [1]. This has been partly motivated by the ubiquity of bilayer membrane vesicles [2] in various natural and industrial systems. Since the lateral size  $L$  of such envelopes is much larger than their thickness, they can be treated to a good approximation as  $(d-1)$ -dimensional manifolds,  $d$  being the embedding dimension. Another consequence of the thinness of the membrane is that it resists stretching much more strongly than bending. Hence, the surface area  $A$  of the membrane is usually assumed fixed. The statistical mechanics of such a manifold involves an interplay between conformational fluctuations and bending elasticity, leading to a characteristic persistence length  $l_p$  [3,4]; over distances smaller than  $l_p$ , the manifold is essentially smooth, whereas beyond it the surface becomes random. When the manifold is closed (a vesicle), its smoothness is affected not only by the elastic persistence length, but also by the degree of swelling (e.g. volume-to-area ratio).

The various studies of vesicle thermodynamics can be classified in two groups according to the volume constraint that they impose (for a given  $A$ ). One body of works, —e.g., Refs. [5–8]—considers the ensemble of fixed volume  $V$ . These studies, aimed at actual bilayer vesicles, assume the low-temperature limit  $l_p > L$ , in which the vesicle is represented by a continuous closed surface in three dimensions (3D). The various equilibrium shapes are derived as ground states of the elastic Helfrich Hamiltonian [7], depending on the dimensionless volume-to-area ratio  $V/A^{3/2}$ . Another body of works treats the ensemble of fixed pressure difference  $p$  across the manifold. The studied systems include Gaussian [9], freely jointed [10,11], and self-avoiding [12–14] rings in 2D, as well as model fluid vesicles in 3D [15–21]. Most of these works assume the random, high-temperature limit ( $l_p \ll L$ ), yet the crossover to  $l_p > L$  was addressed as well [11,12,18,19].

As long as equilibrium averages are concerned, the ensembles of fixed  $V$  and fixed  $p$  are equivalent; i.e., they are related by a smooth, single-valued (Legendre) transform. We focus here on another swelling scenario, where the manifold encapsulates a fixed number  $Q$  of particles while its volume is unconstrained. The interest in such particle-swollen manifolds is not merely theoretical; most actual vesicles are immersed in solution and their membrane, over sufficiently long, experimentally relevant time, is semipermeable, allowing solvent exchange while keeping the solute trapped inside [22–24]. Note that the particle number  $Q$  does not *a priori* imply a certain osmotic pressure, because the manifold is free to change its mean volume and, hence, the mean particle concentration. Nonetheless, since the mean volume and pressure should monotonously increase with  $Q$ , one expects to find equivalence (i.e., certain well-behaved transforms) between the fixed- $Q$  ensemble and the other two. We have recently demonstrated, however, that these ensembles are not equivalent for a freely jointed ring in 2D [25]. A second-order transition between crumpled and swollen states, which occurs in the fixed- $p$  ensemble at a critical pressure  $p_c$  [10], disappears in the fixed- $Q$  case. The criticality is avoided as the system selects such a mean volume that the mean pressure always lies above  $p_c$  for any value of  $Q$ . Thus, the regions of phase space covered in the two ensembles are different.

In the current work we generalize these results, obtaining a unified description for a  $(d-1)$ -dimensional random manifold in  $d$  dimensions, swollen by either a fixed pressure difference or a fixed number of trapped particles. We thereby clarify when the swelling scenarios are thermodynamically equivalent and when they are not. It should be borne in mind that, while the current work is focused on strongly fluctuating, random manifolds ( $L \gg l_p$ ), the bending rigidity and size of real vesicles place them in the low-temperature, smooth regime ( $L < l_p$ ) [26].

We begin in Sec. II with a heuristic scaling analysis, which nevertheless yields the correct qualitative swelling behavior as found in previously studied models. We then proceed to verify these general results using Monte Carlo (MC) simulations of two model manifolds: a self-avoiding ring in 2D (Sec. III), for which the two scenarios are found to be

\*hdiamant@tau.ac.il

equivalent, and a self-avoiding fluid vesicle in 3D (Sec. IV), for which they are not. The results are analyzed and summarized in Sec. V.

## II. SCALING ANALYSIS

We apply a scaling theory [13,27,28] to a closed  $(d-1)$ -dimensional random manifold, composed of  $N$  nodes and embedded in  $d$  dimensions. In response to perturbation (pressure difference  $p$  or  $Q$  noninteracting trapped particles), the manifold is assumed to be divided into subunits, or blobs, containing  $g$  nodes each. The blobs are defined such that each of them stores a tensile energy equal to the thermal energy  $k_B T \equiv 1$  [28],

$$\gamma \xi^{d-1} \sim 1, \quad (1)$$

where  $\gamma$  is the surface tension induced in the manifold due to the perturbation and  $\xi^{d-1}$  is the projected area of a blob. At length scales smaller than the blob size  $\xi$  the manifold is unaffected by the perturbation and assumed to obey the power law

$$\xi^{d-1} \sim g^\nu, \quad (2)$$

where  $\nu$  is a swelling exponent characterizing the unperturbed manifold statistics. At distances larger than  $\xi$  the perturbation stretches the manifold. The total projected area is given by the number of blobs times the projected area per blob,

$$R^{d-1} \sim (N/g) \xi^{d-1}. \quad (3)$$

So far, Eqs. (1)–(3) have been independent of the nature of perturbation ( $p$  or  $Q$ ). The difference between the two cases enters via the Laplace law, which takes the following forms in the fixed- $p$  and fixed- $Q$  ensembles, respectively:

$$\gamma/R \sim p, \quad (4a)$$

$$\gamma/R \sim Q/R^d. \quad (4b)$$

Solution of Eqs. (1)–(3) and (4a) leads to the following power laws for the fixed- $p$  case:

$$\langle V \rangle \sim R^d \sim N^{d/(d-1)} (pN^{1/(d-1)})^{d(1-\nu)/(d\nu-1)},$$

$$\gamma \sim (pN^{1/(d-1)})^{\nu(d-1)/(d\nu-1)}. \quad (5a)$$

(This result, in a different form, has been already obtained in Ref. [15].) Two observations readily follow from Eq. (5a). First, the characteristic pressure difference, required to appreciably swell the manifold (i.e., to obtain  $R \sim N^{1/(d-1)}$ ), scales as  $p \sim N^{-1/(d-1)}$ , regardless of  $\nu$ . This characteristic value reflects the interplay between the mechanical work of inflating an object of volume  $\sim N^{d/(d-1)}$  and the surface entropy of  $N$  degrees of freedom,  $pN^{d/(d-1)} \sim N$ . Second, in cases where  $d\nu=1$  the exponents diverge—i.e., the analysis breaks down—and one expects criticality [13]. Both conclusions are borne out by previously studied models. Gaussian [9] and freely jointed [10] rings, having  $d=2$  and  $\nu=1/2$  (i.e.,  $d\nu=1$ ), behave critically at  $p_c \sim N^{-1}$ , the former swelling to infinite volume and the latter undergoing a second-

order transition to a smooth state. By contrast, self-avoiding rings, with  $d=2$  and  $\nu=3/4$ , swell gradually with  $p$  [12–14].

Turning to the fixed- $Q$  case, we find from Eqs. (1)–(3) and (4b) the power laws

$$\langle V \rangle \sim N^{d/(d-1)} (Q/N)^{d(1-\nu)/(d-1)},$$

$$\gamma \sim (Q/N)^\nu. \quad (5b)$$

The corresponding observations in this case are as follows. First, appreciable swelling occurs for  $Q \sim N$ , regardless of  $\nu$  and  $d$ . Thus, the number of encapsulated particles required to swell the envelope scales with the area only, rather than the volume. This is a consequence of considering a vanishing external pressure [26]. In such a case the particle entropy ( $\sim Q$ ) has to compete only with the surface one ( $\sim N$ ). Second, there is no divergence of exponents in Eq. (5b)—i.e., no criticality. Both conclusions are consistent with findings regarding particle-encapsulating freely jointed rings in 2D [25].

The two blob analyses, along with the resulting power laws [Eqs. (5a) and (5b)], should hold as long as  $1 < g < N$ . This corresponds to the restrictions  $N^{-d\nu/(d-1)} < p < N^{-1/(d-1)}$  and  $1 < Q < N$ . At larger swelling, nonetheless, we expect the manifold to be smooth, having  $\langle V \rangle \sim N^{d/(d-1)}$ . According to Laplace's law this leads to a surface tension  $\gamma \sim pN^{1/(d-1)}$  and  $\gamma \sim Q/N$ . Combining these large-swelling results with Eqs. (5a) and (5b), and provided there is no criticality ( $d\nu \neq 1$ ), we conjecture the following scaling relations, expected to hold for all values of  $p$  and  $Q$ :

$$\langle V \rangle = N^{d/(d-1)} f_p(pN^{1/(d-1)}),$$

$$\gamma = h_p(pN^{1/(d-1)}), \quad (6a)$$

$$\langle V \rangle = N^{d/(d-1)} f_Q(Q/N),$$

$$\gamma = h_Q(Q/N). \quad (6b)$$

The scaling functions for the mean volume,  $f_p$  and  $f_Q$ , should cross over from the power laws of Eqs. (5a) and (5b) for small arguments to constant values for large arguments. The scaling functions for the surface tension,  $h_p$  and  $h_Q$ , are expected to cross over from the power laws of Eqs. (5a) and (5b) to linear ones. The validity of Eqs. (5b) and (6b) has been already proven for a particle-encapsulating freely jointed ring in 2D [25]. In addition, the scaling of Eq. (6a) has been demonstrated in the swelling of those rings with increasing  $p$  above the critical point [10]. We now proceed to check the validity of Eqs. (5a), (5b), (6a), and (6b) in two additional model systems.

## III. SELF-AVOIDING RING IN 2D

We first follow the model and MC scheme presented in Refs. [12–14] for a 2D self-avoiding ring subject to an inflating pressure difference  $p$ . The manifold is represented by a closed chain of  $N$  self-avoiding circles (beads) of diameter  $\sigma = (5/9)l$ , linked by tethers of maximum length  $l \equiv 1$ . In each MC step every bead is moved to a random position

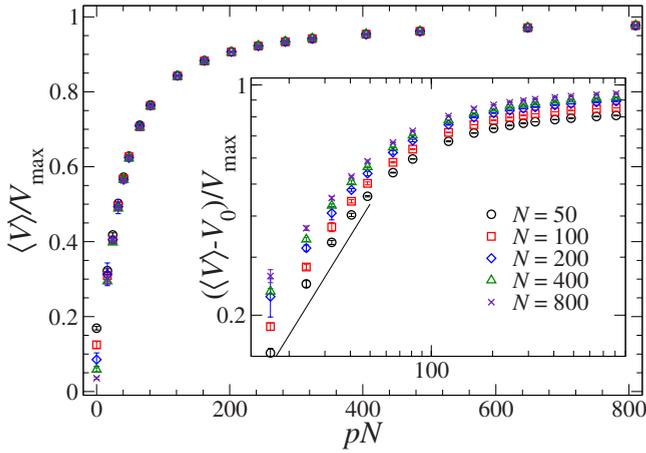


FIG. 1. (Color online) Mean volume of 2D self-avoiding rings as a function of pressure difference. Data were obtained by MC simulations for different ring sizes  $N$  and rescaled according to Eq. (6a),  $V_{\max} = N^2 / (4\pi)$  being the maximum volume of the ring. The inset shows the same data on a log-log scale after the mean volume of the unperturbed ring,  $V_0 \sim N^{3/2}$ , has been subtracted from  $\langle V \rangle$ . A solid line of slope 1 is shown for reference.

within a square of  $(-0.2\sigma, 0.2\sigma)^2$  about its former position. These values of  $\sigma$ ,  $l$ , and maximum step size ensure that self-intersection of the ring cannot occur. The move is weighted by  $W = e^{p\Delta V}$ , where  $\Delta V$  is the difference in (2D) volume of the ring due to the move, and is accepted provided that (i) self-avoidance is fulfilled, (ii) tethers do not exceed their maximum length, and (iii)  $W$  exceeds a random number in the range  $[0, 1]$ . Simulations were performed for  $N = 50 - 800$ .

The mean volume of the ring as a function of pressure difference is presented in Fig. 1. The different data sets collapse onto a single curve once the mean volume is rescaled by the maximum volume of the ring,  $V_{\max} = N^2 / (4\pi)$ , and the pressure by  $N^{-1}$ , in accordance with Eq. (6a). This scaling law, however, yields a vanishing mean volume for  $p = 0$ , whereas the unperturbed ring has a finite mean volume of  $V_0 \sim N^{2\nu}$ ,  $\nu = 3/4$ . In the thermodynamic limit ( $N \rightarrow \infty$ ) the correction is negligible,  $V_0 / V_{\max} \sim N^{-1/2} \rightarrow 0$ , but for finite rings the scaling of Eq. (6a) breaks down for sufficiently small  $p$ , as seen in Fig. 1. Therefore, to capture the initial linear dependence of  $\langle V \rangle$  on  $p$ , as predicted by Eq. (5a) for  $d = 2$  and  $\nu = 3/4$ , we replot in Fig. 1 (inset) the data for  $\langle V \rangle - V_0$ . The initial increase of  $\langle V \rangle - V_0$  with  $p$  seems to be consistent with a linear law, although we cannot claim to have clearly confirmed it.

Next, we turn to particle-encapsulating manifolds by setting  $p = 0$  and introducing  $Q$  ideal particles at random positions inside the ring. Hard-core repulsion is introduced between the particles and envelope beads (but not between the particles themselves), with particle-bead minimum distance of  $\sigma$ . The MC step is extended to include repositioning of each particle within a square of  $(-0.2\sigma, 0.2\sigma)^2$  about its former position. This maximum step size, together with the hard-core repulsion between particles and envelope beads and maximum tether length, ensure that particles cannot exit the ring. Rings of  $N = 50 - 800$  have been simulated, with  $Q$  ranging between 0 and  $20N$ .

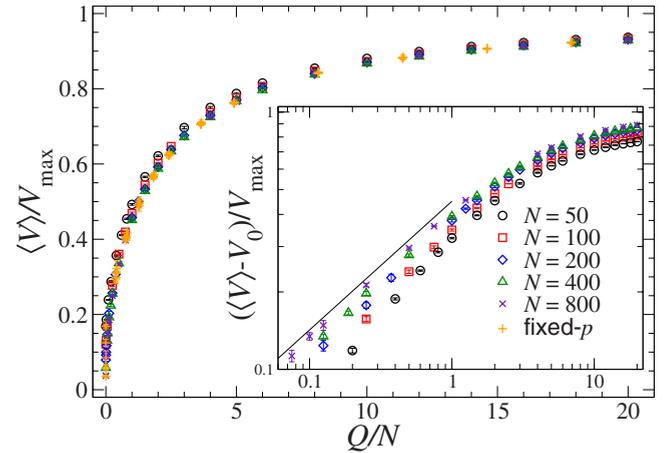


FIG. 2. (Color online) Mean volume of 2D self-avoiding rings as a function of number of encapsulated particles. Data were obtained by MC simulations for different ring sizes  $N$  and rescaled according to Eq. (6b),  $V_{\max} = N^2 / (4\pi)$  being the maximum volume of the ring. Also plotted are the data points from the fixed- $p$  simulation (Fig. 1), whose horizontal coordinate is calculated as  $p\langle V(p) \rangle / N$ . The inset shows the data on a log-log scale after the mean volume of the unperturbed ring,  $V_0 \sim N^{3/2}$ , has been subtracted from  $\langle V \rangle$ . A solid line of slope  $1/2$  is shown for reference.

In Fig. 2 we present the mean volume as a function of  $Q$ . In agreement with Eq. (6b) all data collapse onto a single curve when  $\langle V \rangle$  is scaled by  $N^2$  and  $Q$  by  $N$ . As in the case of fixed  $p$ , discussed above, scaling breaks down for very small  $Q$  when  $\langle V \rangle$  becomes affected by the finite volume of the unperturbed state. The power law predicted by Eq. (5b) for 2D self-avoiding rings ( $d = 2$ ,  $\nu = 3/4$ ),  $\langle V \rangle \sim V_{\max} (Q/N)^{1/2}$ , is nevertheless verified after subtracting  $V_0$  from the mean volume (Fig. 2, inset).

To demonstrate the equivalence of the fixed- $p$  and fixed- $Q$  scenarios for this system we transform the data for pressurized rings (Fig. 1) according to  $Q(p) = p\langle V(p) \rangle$  and present them in Fig. 2 alongside the data for fixed  $Q$ . The data sets of the two scenarios match nicely over the entire ranges of  $p$  and  $Q$ .

#### IV. SELF-AVOIDING FLUID VESICLE IN 3D

The second manifold we consider is a discrete model of a fluid vesicle, which was extensively studied by MC simulations under fixed pressure difference  $p$  [15–20]. The vesicle is represented by a closed, triangulated, off-lattice network of  $N$  nodes (self-avoiding spheres) of diameter  $\sigma = l / \sqrt{2}$ , interconnected by a fixed number of tethers of maximum length  $l \equiv 1$ . Membrane fluidity is mimicked by constantly varying the network connectivity. The MC step comprises two parts. (i) Each bead is moved randomly within a cube of  $(-0.1\sigma, 0.1\sigma)^3$  about its former position (self-avoidance permitting). The move is weighted by a Boltzmann factor of  $e^{p\Delta V}$ , where  $\Delta V$  is the change in volume caused by the move. (ii)  $N$  attempts are made to break a randomly chosen tether, which has formed the common side of two triangles, and rebuild it between the two other corners of those triangles (provided that the required tether length does not exceed  $l$ ).

The choice of  $\sigma$ ,  $l$ , and maximum step size prevents a bead from passing through another part of the network, making the manifold self-avoiding.

The swelling of this model vesicle as a function of  $p$  follows three regimes [15]. (i) At low pressures the vesicle is in a collapsed state, having branched-polymer statistics, where the mean volume and mean-square radius of gyration scale as  $\langle V \rangle \sim R^2 \sim N$ , with negligible dependence on  $p$  [15,29–31]. (ii) At a critical pressure,  $p = p^*(N)$ , the vesicle undergoes a first-order transition to a swollen state, whose mean volume gradually increases with  $p$  as  $\langle V \rangle \sim p^{0.47} N^{1.73}$  [15]. (iii) At sufficiently large  $p$  the power-law behavior crosses over to asymptotic swelling toward the maximum volume.

The blob analysis presented in Sec. II obviously fails in regime (i) of low swelling, since the volume enclosed in such collapsed manifolds does not follow the standard relation  $\langle V \rangle \sim R^d$ . Instead, we use the fact that the ratio between the cross-section (frame) area of the manifold and its real surface area is vanishingly small. Such a manifold has a constant surface tension,  $\gamma \sim 1$  (in units of  $k_B T/l^2$ ) [32]. Applying Laplace's law,  $p \sim \gamma/R \sim N^{-1/2}$ , we find that the deflated regime (i) is valid for  $p \lesssim N^{-1/2}$ ; i.e.,

$$p \lesssim N^{-1/2}: \quad \langle V \rangle \approx V_0 \sim N. \quad (7)$$

In regime (ii) the scaling analysis of Sec. II holds. Comparison of the previously obtained power law,  $\langle V \rangle \sim p^{0.47} N^{1.73}$ , with Eq. (5a) for  $d=3$ , gives  $\nu=0.787$  [15]. Our modified scaling analysis [Eqs. (5a) and (6a)] indicates that  $p$  is scaled with  $N^{-1/2}$ . We note that the power-law dependence of the critical pressure  $p^*$  on  $N$  has been controversial [19], with exponents ranging between  $-0.5$  [16] and  $-0.69$  [20]. The scaling argument for  $p > p^*$ , together with Eq. (7) for  $p < p^*$ , strongly suggest that  $p^* \sim N^{-1/2}$  [33].

We have repeated the MC simulations for fixed  $p$ , as presented in Ref. [15], while extending them to larger vesicles and higher pressure values. The results are shown in Fig. 3, scaled according to Eq. (6a). The first-order transition at  $p^* \sim N^{-1/2}$  is clearly reproduced, and the predicted scaling for the entire range of  $p > p^*$  is confirmed. The scaling for  $p \geq p^*$  is not inconsistent with the power law of Ref. [15] and Eq. (5a), having  $\nu$  between 0.7 and 0.8 (Fig. 3, inset), yet this regime is too narrow to be clearly resolved.

We now turn to particle-encapsulating vesicles. Repeating the aforementioned argument for the deflated state of regime (i),  $Q/\langle V \rangle \sim \gamma/R \sim N^{-1/2}$ , we find

$$\langle V \rangle \sim N^{3/2}(Q/N). \quad (8)$$

(This linear dependence of  $\langle V \rangle$  on  $Q$  will be shown in Sec. V to be intimately related to the phase transition observed as a function of  $p$ .) The scaling law of Eq. (8) for the low-swelling regime turns out to be similar to that of Eq. (5b). Hence, despite the inadequacy of the blob analysis in regime (i), we expect the scaling conjecture, Eq. (6b), to hold for all values of  $Q$  in this model as well.

To check these predictions we modified the MC scheme presented above by setting  $p=0$  and adding  $Q$  ideal particles of diameter  $\sigma$ , randomly positioned inside the vesicle. The

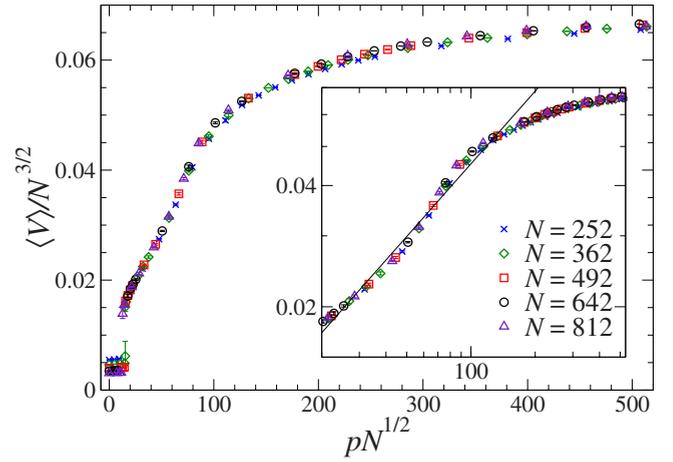


FIG. 3. (Color online) Mean volume of 3D self-avoiding fluid vesicles as a function of pressure difference, as obtained by MC simulations for different vesicle sizes  $N$ . Data are scaled according to Eq. (6a), exhibiting a discontinuous transition at  $p^* \sim N^{-1/2}$ . For  $p > p^*$  the data collapse onto a single curve. The inset presents the same data for  $p > p^*$  on a log-log scale. A solid line of slope 0.6 (corresponding to  $\nu=0.75$ ) is shown for reference.

particles do not interact with each other, but have a hard-core repulsion with the network nodes, keeping them trapped inside the vesicle. The MC step is extended to include random repositioning of each particle within a cube of  $(-0.1\sigma, 0.1\sigma)^3$  about its former position. Vesicles with  $N$  ranging between 162 and 642 and  $Q$  up to  $10N$  (for the smallest vesicle) have been simulated.

Results for the mean volume as a function of  $Q$  for various vesicle sizes are shown in Fig. 4. Once the volume  $V_0$  of the unperturbed (branched) state [Eq. (7)], which is inaccessible to particles due to their excluded-volume interaction with the manifold, is subtracted from  $\langle V \rangle$ , the data collapse onto a single curve according to Eq. (6b). Two power-law regimes are seen in Fig. 4 (inset). At low swelling  $\langle V \rangle$  increases linearly with  $Q$ , in agreement with Eq. (8) [34]. At about  $Q \approx 0.08N$  the swelling crosses over to a different power law which, when fitted to Eq. (5b), yields  $\nu=0.75(2)$ . This value is close to that found in the fixed- $p$  simulations,  $\nu=0.787$  [15,35]. For larger values of  $Q$  this power-law regime should cross over to asymptotic saturation toward the maximum volume. Because of computer limitations we could sample only the lowest edge of this regime (Fig. 4, inset).

Unlike the case of fixed  $p$ , the vesicle gradually swells with  $Q$ , exhibiting no phase transition. To further verify the absence of a first-order transition we have measured the probability distribution function of the volume,  $P(V)$ , as a function of  $Q$ . Whereas under fixed  $p$ , at  $p=p^*$ , one finds a bimodal distribution [Ref. [15] and Fig. 5(a)]—i.e., coexistence of collapsed and swollen states—for particle-encapsulating vesicles we obtain unimodal distributions for all values of  $Q$  [Fig. 5(b)].

Finally, let us consider the effective pressure exerted by the encapsulated ideal particles,  $p=Q/\langle V \rangle$ . From Eq. (6b) we have

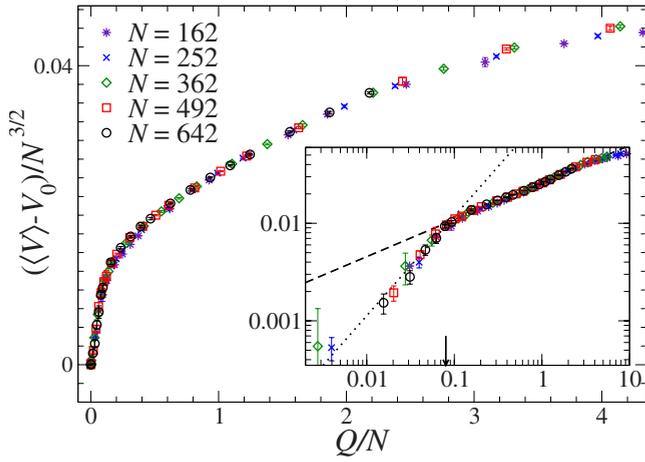


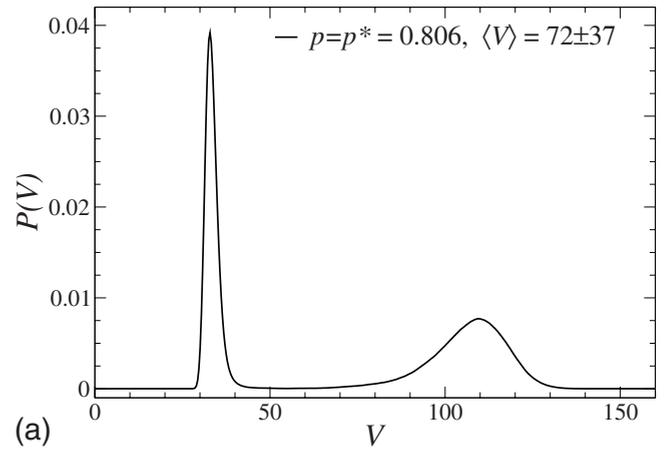
FIG. 4. (Color online) Mean volume of 3D self-avoiding fluid vesicles as a function of the number of trapped particles, as obtained by MC simulations for different vesicle sizes  $N$ . Data collapse onto a single curve according to Eq. (6b) once the volume of the unperturbed vesicle,  $V_0 \sim N$ , is subtracted from  $\langle V \rangle$ . The inset represents the same data on a log-log scale, exhibiting a linear regime for  $Q \leq N$ ,  $(\langle V \rangle - V_0)/N^{3/2} \sim (Q/N)^{1.02(3)}$  (dotted line), followed by a more swollen regime with  $(\langle V \rangle - V_0)/N^{3/2} \sim (Q/N)^{0.38(3)}$  (dashed line). The arrow indicates the crossover between the two regimes at  $Q \approx 0.08N$ .

$$p = N^{-1/2} \psi(Q/N), \quad \psi(x) = x/f_Q(x). \quad (9)$$

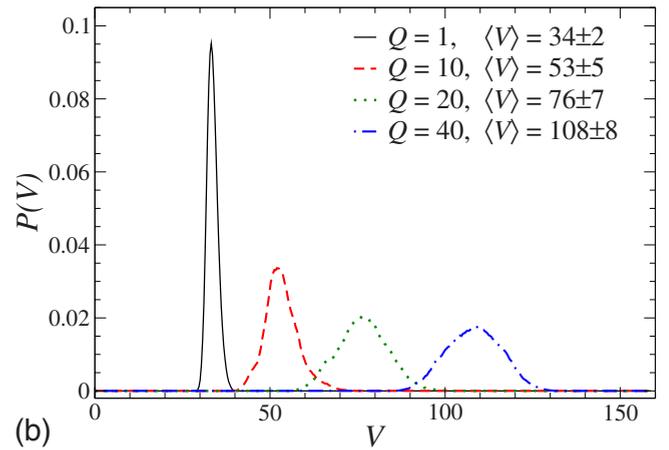
In the low-swelling regime we have found a linear behavior,  $f_Q(x \ll 1) \sim x$  [Eq. (8) and Fig. 4, inset]. Thus,  $\psi(x \ll 1) = \text{const}$ ; i.e., the effective pressure does not change with  $Q$  throughout this regime. Figure 6 demonstrates the data collapse according to Eq. (9), as well as the finite, constant pressure  $p_{\min}$  at low swelling even for the smallest values of  $Q$ . (In calculating the concentration and pressure from the simulations we have considered the particle-accessible volume,  $\langle V \rangle - V_0$ .) One expects  $p_{\min}$  to coincide with the transition value under fixed pressure,  $p^*$ . [Compare also Fig. 5(a), plotted for  $p = p^*$ , with Fig. 5(b), where the effective pressure is essentially fixed at  $p_{\min}$  for all curves.] We find, however,  $p^* \approx 1.8p_{\min}$ . This discrepancy may stem from the interaction of the particles with the vesicle, making them deviate from the ideal-gas behavior, particularly in the deflated state.

## V. DISCUSSION

The scaling analysis presented in Sec. II yields a unified account of the swelling of random manifolds with increasing pressure difference or number of encapsulated particles. The validity of this description has been demonstrated for several model systems in Secs. III and IV and in Ref. [25]. Similar scaling analyses for the case of fixed  $p$  were previously presented in Refs. [13,15]. Those analyses and ours coincide in the power-law regime, Eq. (5a). However, while the previous analyses are focused on the weak-swelling regime and constructed to include the random, unperturbed state of the manifold, the one presented here is aimed at encompassing the high-swelling behavior. Thus, on the one hand, our scaling relations, Eqs. (6a) and (6b), cannot account for the un-



(a)



(b)

FIG. 5. (Color online) Volume distribution functions of 362-node 3D vesicles. (a) For fixed pressure difference, at the transition point, the distribution is bimodal. (b) Under fixed number of encapsulated particles the distribution is always unimodal.

perturbed state and give a vanishing mean volume in the limit of vanishing perturbation. The range of  $p$  (or  $Q$ ) where this deficiency is relevant, nonetheless, vanishes in the thermodynamic limit [36]. On the other hand, whereas the previous analyses assumed that scaling broke down at sufficiently large swelling [13,15], we have claimed that Eqs. (6a) and (6b) should hold for the entire range of  $p$  or  $Q$ . Although there is *a priori* no reason why the scaling behavior should have this broad range, we analytically proved the conjecture for freely jointed rings in 2D at fixed  $p > p_c$  [10] or fixed  $Q$  [25]. In the current work we have provided further numerical support of the scaling conjecture in several additional systems: 2D self-avoiding rings at fixed  $p$  or fixed  $Q$  and 3D fluid vesicles at fixed  $p > p^*$  or fixed  $Q$ . Hence, provided that the swelling exhibits no criticality, the scaling relations, Eqs. (6a) and (6b), seem to be applicable in a broad range of systems.

The analysis presented here for the swelling with  $Q$  yields new scaling relations, which have been confirmed in all studied systems. The different behavior of particle-encapsulating manifolds lies in the response of manifold volume to changes

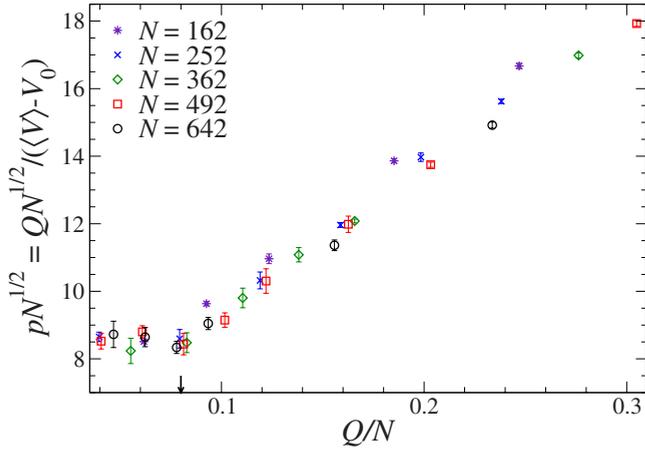


FIG. 6. (Color online) Effective pressure of encapsulated particles as a function of particle number, as obtained by MC simulations for various vesicle sizes  $N$ . Data collapse according to Eq. (9). Note the finite effective pressure at small  $Q$ . The arrow indicates the crossover between the two swelling regimes at  $Q \approx 0.08N$ .

in the number of encapsulated particles. The resulting particle concentration and effective pressure depend on this response and, therefore, may have a nontrivial dependence on  $Q$ . In certain cases this may lead to thermodynamic inequivalence of the fixed- $p$  and fixed- $Q$  ensembles. Equivalence breaks down when the two ensembles are no longer related by a one-to-one smooth transform. In the two examples where inequivalence has been demonstrated—2D freely jointed rings [25] and 3D fluid vesicles (Sec. IV)—both conditions of smoothness and single-valuedness are violated: (i) a criticality in the fixed- $p$  ensemble makes the transform  $Q(p) = p\langle V(p) \rangle$  nonanalytic, and (ii) the effective pressure in the fixed- $Q$  ensemble is bounded from below by a finite value; i.e., states of low pressure are inaccessible (cf. Fig. 6). We now show that this combination of criticality under fixed  $p$  and inaccessible states for fixed  $Q$  is not a coincidence.

Let us consider a general power-law response to particle number,  $\langle V \rangle \sim Q^\alpha$ . Transforming to the fixed- $p$  ensemble, we get  $p(Q) = Q/\langle V \rangle \sim Q^{1-\alpha}$  and  $\langle V \rangle \sim p^{\alpha/(1-\alpha)}$ . Several observations follow from these relations. First, thermodynamic stability dictates that  $\langle V \rangle$  increase with  $p$ —i.e.,  $\alpha \leq 1$ . We are left with two different cases. (i) If  $\alpha < 1$ , there is no criticality and arbitrarily small values of  $Q$  will correspond to arbitrarily small values of  $p$ . Hence, in this case there is equivalence. (ii) If  $\alpha = 1$ , we expect both criticality under fixed  $p$  and inaccessibility of small-pressure states at fixed  $Q$ —i.e., inequivalence of the two swelling scenarios. For maximum  $\alpha$ , the manifold volume is maximally susceptible to changes in  $Q$  (linear in  $Q$ ), to the extent that the concentration and pressure do not change with  $Q$  (cf. Fig. 6). Thus, criticality and inequivalent phase spaces come hand in hand. In a standard case, where the blob analysis of Sec. II holds, we get from Eq. (5b)  $\alpha = d(1-\nu)/(d-1)$ , and the condition  $\alpha \leq 1$  is equivalent to  $d\nu \geq 1$ . In addition, one has a geometrical lower bound for the swelling exponent, which cannot be smaller than that of a folded, compact manifold,  $\nu \geq (d-1)/d$ . This leads to the restriction  $\alpha \leq 1/(d-1)$ , which is consistent with, and stricter than, the thermody-

amic one,  $\alpha \leq 1$ . Hence, we conclude that for most systems, which obey the analysis of Sec. II, case (ii) above, involving criticality and inequivalence, can occur only in 2D—i.e., for  $d=2$  and  $\nu=1/2$  [10,25].

All of these general conclusions are supported by specific examples. A 2D self-avoiding ring is an example of case (i) above. It obeys the scaling analysis of Sec. II with  $d=2$ ,  $\nu=3/4$ —i.e.,  $\alpha=1/2$ . (The value of  $\alpha$  has been confirmed by simulations; see Fig. 2.) This system exhibits no criticality under fixed  $p$ , and the two ensembles have been found equivalent (Fig. 2). The more interesting case (ii) has been encountered in three systems. Two examples are provided by Gaussian and freely jointed rings in 2D [25]. For both examples the blob analysis holds, and  $d=2$ ,  $\nu=1/2$  (i.e.,  $d\nu=1$ ). The third example of the anomalous case (ii) is a 3D fluid vesicle (Sec. IV), for which the blob analysis of Sec. II fails, yet a linear dependence of  $\langle V \rangle$  on  $Q$  has been found [Eq. (8) and Fig. 4]. Indeed, under fixed  $p$  [9,10,15] all three examples exhibit phase transitions.

This host of examples leads to the expectation that the picture described here, including the scaling relations and possible phase transitions, should hold for any random manifold swollen by either a pressure difference or encapsulated particles. In cases where the blob analysis of Sec. II is valid, one needs to know merely the dimensionality  $d$  and the statistics of the unperturbed manifold ( $\nu$ ) to predict the qualitative swelling behavior. In other, exceptional cases (e.g. the 3D fluid vesicle of Sec. IV) it suffices to know the response of the unperturbed manifold to a small number of encapsulated particles (i.e.,  $\alpha$ ).

The thermodynamic inequivalence between the fixed- $p$  and fixed- $Q$  scenarios, reported above for certain systems, also implies inequivalence between the canonical and grand-canonical ensembles in those systems. This is because fixing the chemical potential  $\mu$  of the encapsulated particles inevitably fixes also the mean pressure  $p$  that they exert on the manifold, as these two intensive variables are related via the particles' equation of state. (For example, for ideal particles  $\mu = \ln p$ .) Once again, because of the unconstrained volume, the system cannot attain arbitrarily small concentrations as  $Q$  is decreased, and, therefore, the full range of  $\mu$  is not covered. The inequivalence of the fixed- $Q$  and fixed- $\mu$  ensembles has been directly demonstrated for freely jointed 2D rings [25].

In the current work we have not explicitly considered the bending rigidity of the vesicle. Such a bending-free description is valid in two limits: (i) At sufficiently strong swelling the fluctuations of any vesicle are governed by surface tension rather than bending rigidity. (ii) If the manifold is sufficiently large ( $L \gg l_p$ ), bending rigidity merely renormalizes the molecular length  $a$  to  $l_p$  and the number of surface degrees of freedom  $N$  to  $Na^2/l_p^2$ . It is this random, strongly fluctuating case which has been the focus of the current work. On the one hand, due to their bending rigidity ( $\kappa \sim 10k_B T$ ) and size (0.1–10  $\mu\text{m}$ ), real bilayer vesicles are smooth and do not satisfy limit (ii). On the other hand, some of our most significant results (e.g., the inaccessibility of low-pressure states) concern weak swelling, outside limit (i), where the bending rigidity of real vesicles plays an important role. Thus, the direct relevance of the current work to real

bilayer vesicles is limited. Yet, overall, this work and the specific examples associated with it highlight the qualitative differences which may emerge between pressurized manifolds and particle-encapsulating ones. Indeed, the different behavior of particle-encapsulating vesicles is manifest also in realistic scenarios involving smooth membranes—e.g., highly swollen bilayer vesicles in solution [26].

## ACKNOWLEDGMENTS

We thank D. Harries for helpful discussions. Acknowledgment is made to the Donors of the American Chemical Society Petroleum Research Fund for support of this research (Grant No. 46748-AC6).

- 
- [1] *Statistical Mechanics of Membranes and Surfaces*, edited by D. Nelson, T. Piran, and S. Weinberg (World Scientific, Singapore, 1989).
- [2] S. A. Safran, *Statistical Thermodynamics of Surfaces, Interfaces, and Membranes* (Addison-Wesley, Reading, MA, 1994).
- [3] P.-G. de Gennes and C. Taupin, *J. Phys. Chem.* **86**, 2294 (1982).
- [4] R. Lipowsky, *Nature (London)* **349**, 475 (1991).
- [5] U. Seifert, *Adv. Phys.* **46**, 13 (1997).
- [6] P. B. Canham, *J. Theor. Biol.* **26**, 61 (1970).
- [7] W. Helfrich, *Z. Naturforsch. C* **28**, 693 (1973).
- [8] U. Seifert, K. Berndl, and R. Lipowsky, *Phys. Rev. A* **44**, 1182 (1991).
- [9] J. Rudnick and G. Gaspari, *Science* **252**, 422 (1991); G. Gaspari, J. Rudnick, and A. Beldjenna, *J. Phys. A* **26**, 1 (1993).
- [10] E. Haleva and H. Diamant, *Eur. Phys. J. E* **19**, 461 (2006).
- [11] M. K. Mitra, G. I. Menon, and R. Rajesh, *Phys. Rev. E* **77**, 041802 (2008).
- [12] S. Leibler, R. R. P. Singh, and M. E. Fisher, *Phys. Rev. Lett.* **59**, 1989 (1987).
- [13] A. C. Maggs, S. Leibler, M. E. Fisher, and C. J. Camacho, *Phys. Rev. A* **42**, 691 (1990).
- [14] C. J. Camacho and M. E. Fisher, *Phys. Rev. Lett.* **65**, 9 (1990).
- [15] G. Gompper and D. M. Kroll, *Phys. Rev. A* **46**, 7466 (1992).
- [16] G. Gompper and D. M. Kroll, *Europhys. Lett.* **19**, 581 (1992).
- [17] D. M. Kroll and G. Gompper, *Science* **255**, 969 (1992).
- [18] G. Gompper and D. M. Kroll, *Phys. Rev. Lett.* **73**, 2139 (1994); *Phys. Rev. E* **51**, 514 (1995).
- [19] G. Gompper and D. M. Kroll, *J. Phys.: Condens. Matter* **9**, 8795 (1997).
- [20] B. Dammann, H. C. Fogedby, J. H. Ipsen, and C. Jeppesen, *J. Phys. I* **4**, 1139 (1994).
- [21] A. Baumgartner, *Physica A* **190**, 63 (1992).
- [22] J. Käs and E. Sackmann, *Biophys. J.* **60**, 825 (1991).
- [23] J. Nardi, R. Bruinsma, and E. Sackmann, *Phys. Rev. Lett.* **82**, 5168 (1999).
- [24] P. Peterlin and V. Arrigler, *Colloids Surf., B* **64**, 77 (2008); P. Peterlin, G. Jaklič, and T. Pisanski, e-print arXiv:0804.2316.
- [25] E. Haleva and H. Diamant, *Eur. Phys. J. E* **21**, 33 (2006); **25**, 223(E) (2008).
- [26] E. Haleva and H. Diamant, *Phys. Rev. Lett.* **101**, 078104 (2008).
- [27] P.-G. de Gennes, *Scaling Concepts in Polymer Physics* (Cornell University Press, New York, 1979).
- [28] P. Pincus, *Macromolecules* **9**, 386 (1976).
- [29] C. F. Baillie and D. S. Johnston, *Phys. Lett. B* **283**, 55 (1992).
- [30] D. H. Boal and M. Rao, *Phys. Rev. A* **45**, R6947 (1992).
- [31] D. M. Kroll and G. Gompper, *Phys. Rev. A* **46**, 3119 (1992).
- [32] F. David and S. Leibler, *J. Phys. II* **1**, 959 (1991).
- [33] Similarly, the critical pressure in 2D Gaussian and freely jointed rings was analytically found to scale as  $N^{-1/(d-1)} \sim N^{-1}$  [9,10].
- [34] Artificially attempting to extract  $\nu$  for the low-swelling regime by fitting these results to Eq. (5b), one gets the unphysical value of  $\nu=1/3$ , which is smaller than the lower bound of  $2/3$  set by a fully collapsed, compact manifold. This highlights the necessity of a different scaling analysis in this regime, as presented in Sec. IV.
- [35] We note that this value of  $\nu$  is also suspiciously close to the one known for self-avoiding polymerized (i.e., solid) 3D manifolds,  $\nu \approx 0.8$ . See Y. Kantor, in *Statistical Mechanics of Membranes and Surfaces* [1], pp. 111–130. This suggests that the configurations of the variable-connectivity (fluid) manifold studied here, when it is sufficiently swollen, may become statistically equivalent to those of polymerized membranes. However, we currently cannot prove this suggestion.
- [36] The relevant range in the fixed- $p$  ensemble is  $pN^{1/(d-1)} < N^{(1-d\nu)/(d-1)}$ , which vanishes as  $N \rightarrow \infty$  for  $d\nu > 1$ —i.e., as long as there is no criticality. In the fixed- $Q$  case the range is  $Q/N < 1/N$ , which is irrelevant regardless of  $\nu$ .