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## Statistical Thermodynamics of Pressurized and Particle-Encapsulating Vesicles

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# Abstract

Vesicles are closed fluctuating compartments, whose envelope is a lipidic bilayer membrane. Due to the amphiphilic nature of the lipid molecules, once in an aqueous solution, they self-assemble to form a membrane, which is semipermeable — while small non-ionic molecules permeate relatively easily through this membrane in or out of the vesicle, the permeation of bigger or ionic molecules is hindered. As a consequence, solvent diffusion may change the vesicle volume, while solute particles trapped inside the vesicle exert pressure on the membrane.

In this thesis we study the statistical thermodynamics of vesicle swelling in two scenarios — that of a fixed inflating pressure difference and that of vesicles encapsulating a fixed number of particles. While the first case was previously investigated in several studies, the second one is addressed here in detail for the first time. A *particle-encapsulating vesicle* is a unique system, which has no constraint on its volume, neither directly by fixing the volume, nor by a Lagrange multiplier p. Although this object has a mean volume, which depends on the number of trapped particles, the resulting thermodynamic ensemble is not necessarily equivalent to that of fixed pressure difference — fixing the number of particles does not imply *a priori* a certain osmotic pressure, because the manifold is free to change its mean volume and, hence, the mean particle concentration. In other words, both the volume and pressure difference fluctuate.

The investigation begins with general scaling analyses for the swelling of random manifolds in the two scenarios. These analyses yield scaling laws, which relate the mean volume of the vesicle to the pressure difference or to the number of trapped particles. It is shown that, while the swelling with pressure difference might undergo a criticality, that of particle-encapsulating random manifolds is always gradual with the number Q of trapped particles. This analysis demonstrates the difference between the two ensembles and serves as a guideline along the thesis, where a statistical mechanics investigation of several specific models is conducted.

The first model is that of a closed two-dimensional freely jointed chain, *i.e.*, an ideal inextensible ring, in the fixed-p and fixed-Q ensembles. This system is treated using a Flory argument, a mean-field calculation of the partition function, and Monte Carlo simulations. All three methods show that in the fixed-p ensemble the ring undergoes a continuous transition from a crumpled random-walk-like phase to a smooth one. This transition disappears when the swelling is caused by a fixed number of trapped particles, where the vesicle swells gradually, following a single scaling law. In the limit of highly swollen rings, exact expressions relating the mean volume to p or Q are obtained.

We then continue to a two-dimensional self-avoiding ring. We treat both pressurized and particle-encapsulating rings using Monte Carlo simulations. The obtained data is consistent with the scaling analyses and yield a gradual swelling in both scenarios and the two scenarios are shown to be thermodynamically equivalent for this model.

A third model, of a three-dimensional particle-encapsulating fluid vesicle, is studied using Monte Carlo simulations, and the results are compared to those of a previously studied similar system subject to a pressure difference. While the swelling with pressure difference undergoes a first-order transition, the swelling with increasing number of particles particles is gradual, *i.e.*, the ensembles are inequivalent for this model system.

Finally, we consider a ubiquitous scenario where a fluctuating, semipermeable vesicle is immersed in a solution while enclosing a fixed number of solute particles. Assuming that the vesicle has a maximum volume, we show that its swelling with increasing number of trapped particles exhibits a continuous phase transition from a fluctuating state to the maximum-volume configuration. Beyond the transition vesicle fluctuations are suppressed and appreciable pressure difference and surface tension build up. This criticality is unique to particle-encapsulating vesicles and is absent when the swelling is caused by a controlled pressure difference. It implies a universal swelling behavior of vesicles as they approach their limiting volume and osmotic lysis.

Overall, the scaling analysis and host of examples studied in this thesis emphasize the qualitative differences which may emerge between pressurized manifolds and particle-encapsulating ones. Beside the theoretical interest in these systems, the observations may be also of practical importance, since particle-encapsulating vesicles are the common scenario in nature and industrial applications.

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# Chapter 1 General Introduction

Biological membranes are flexible surfaces which have a crucial role in nature. They form a limiting envelope for every living cell as well as for some types of viruses. The compartment of the cell, as well as that of a cell organelle, is defined by a bilayer membrane vesicle, which functions as a selective barrier between the interior and exterior. Vesicles are also widely used in industrial applications for cosmetics and drug delivery. From a physical point of view, membranes belong to the class of *soft condensed matter*, that is, condensed matter, which is neither a simple liquid nor an ordered solid. A major breakthrough in the field of soft-matter physics was achieved by de Gennes in his works on polymers and liquid crystals, for which he received the Nobel prize in 1991. The study of membrane statistical thermodynamics, at least in the way it is conducted along this thesis, is closely related to the principles and scaling methods developed by de Gennes and others soft-matter theorists for strongly fluctuating systems (e.g., polymers in solution).

The aim of this chapter is to give a brief overview of the statistical thermodynamics of membranes and the established methods used in this field, focusing on issues and methods that will be useful in later chapter of this thesis. The first section (Section 1.1) presents some of the theoretical tools used in the field of polymer physics and examines several analytical approaches as well as Monte Carlo simulations. Section 1.2 extends these tools to the membranal case and discusses other theoretical models used in membrane research.

## 1.1 Polymers

Polymers are chain-like molecules composed of covalently connected repeat units called monomers. Man-produced polymers surround our everyday life. Common examples are plastic and rubber, but synthetic polymers (*e.g.*, Nylon, Dacron, Teflon, Celluloid) are actually incorporated in most products including those of the food industry. Polymers also appear in nature; the most prominent example is DNA molecules, which exist in every living organism as well as in viruses and carry the genetic code. Other biological examples include proteins, polysaccharides, and actin and myosin filaments. (The last two examples are polymers whose repeat unit is a protein — a polymer by itself.)

While the implementation of polymer science leads to a variety of unique materials, the theoretical study of this field is related to diverse and fascinating areas of physics and mathematics such as critical phenomena and the world of fractals.

## 1.1.1 Freely Jointed Chain

The most naive description of a polymer chain is that of a freely jointed model, also called the ideal chain model. In such a description there is no interaction between monomers and thus link directions are uncorrelated. In other words, one might say that the angle  $\theta$  between two links could be chosen from  $[0, 2\pi]$  with uniform probability (including  $\theta = \pi$  !).<sup>1</sup> Obviously, this model is not physical. To start with, it does not include an excluded volume interaction between monomers. Furthermore, in its simplified formalism, it does not take into account the bending modulus of the polymeric chain. (We will address these two issues in the following subsections.) Nevertheless, the ideal chain model is a good description for polymers in theta-solvents [1], for which the monomer–monomer interaction is similar to the monomer–solvent one. Also, due to the simplicity of the model, calculations are more easily performed and the obtained analytical results may serve as a limiting case, with which more detailed models can be compared.

The freely jointed chain description is analogous to random walks [2, 3], and thus,

<sup>&</sup>lt;sup>1</sup>Actually, to describe the conformation of a polymer embedded in three dimensions one should define, for each two successive links, a torsion angle as well.

for long enough chains the polymer's end-to-end distance (random walk displacement) R is related to the number of monomers (steps) N by

$$\langle \mathbf{R}^2 \rangle \sim N^{2\nu} l^2, \quad \nu = 1/2, \tag{1.1}$$

where l is the monomer–monomer link length (step size). The exponent  $\nu$  is called, in polymer physics, the swelling exponent, and for random walk statistics its value is  $\nu = 1/2$  for any embedding dimension [3].

The probability density function of the end-to-end distance is also known from random walk theories to be,

$$P(\mathbf{R}) = \left(\frac{3}{2\pi N l^2}\right)^{3/2} e^{-3\mathbf{R}^2/(2Nl^2)}.$$
 (1.2)

This probability density function holds only for end-to-end distances much smaller than the total chain length,  $|\mathbf{R}| \ll Nl$ .

The free energy of a polymer chain for a given end-to-end distance R, up to a constant prefactor, is simply given by

$$F(\mathbf{R}) = -k_{\rm B}T\log P(\mathbf{R}) = 3k_{\rm B}T\mathbf{R}^2/(2Nl^2) + \text{const},$$
(1.3)

which is sometime referred to as the entropic spring. To say it differently, holding both ends of the polymer and pulling them to a distance R one from the other is analogous to stretching a harmonic spring, having a spring constant  $3k_{\rm B}T/(Nl^2)$ , by R.

For closed chains, which are the focus of Chapters 3 and 4, the end-to-end distance is R = 0. To characterize their size, we must use a different quantity—the radius of gyration  $R_{\rm g}$ , which is defined as the root-mean-square distance of monomers from the center of mass of the chain. It is this property, rather than the end-to-end distance, which is measured by scattering experiments on polymers. It is quite simple to show that for open ideal chains, the radius of gyration follows the same statistics as the end-to-end distance,  $R_{\rm g}^2 \sim \langle \mathbf{R}^2 \rangle \sim N$ , and for ideal closed chains we have simply  $R_{\rm g}^2 \sim N$  [1].

The swelling exponent  $\nu = 1/2$  is sometimes referred to as the mean-field swelling exponent, also due to the analogy between polymers and critical phenomena [4]. In this analogy, approaching the critical temperature,  $T - T_c \rightarrow 0$  (in a system undergoing a continuous phase transition), is analogous to taking the thermodynamic limit  $1/N \to 0$ (in a polymeric system). The correlation length, which diverges as  $\xi \sim |T - T_c|^{-\nu}$  at the critical point, is analogous to the radius of gyration,  $R_g \sim N^{\nu}$ . In the mean-field universality class, the critical exponent  $\nu$  is 1/2 [5], which is equal to the swelling exponent of an ideal chain. Further discussion of this analogy is found in de Gennes' book [4].

### **1.1.2** Chemical Constraints and Semiflexible Chains

Real polymers, however, do not obey the simple ideal chain model and their link directions are correlated. This may have several explanations. In a chemical-microscopic view, the angle between links  $\theta$  has a nonuniform distribution. (See, for example, the Ramachandran distribution for protein backbone angles [6].) In many polymers  $\theta$  is roughly fixed. On a different level, a physical-macroscopic description will incorporate a resistance of the chain to bending, *i.e.*, bending rigidity  $\kappa$ . Both explanations suggest that there *is* correlation along the chain, which decays after a sufficient number of repeat units or, equivalently, beyond a sufficient large distance along the chain contour. This distance is called the Kuhn length. Since links become uncorrelated beyond this distance, it is possible to return to the ideal chain description by redefining the number *n* of (Kuhn) monomers and (Kuhn) link length *b* as follows,

$$n = Nl/b,$$
  
$$b = \langle \mathbf{R}^2 \rangle / (Nl). \tag{1.4}$$

For sufficiently long chains, b does not depend on N and is an intrinsic property of the polymer. The swelling thus obeys,

$$\langle \mathbf{R}^2 \rangle = n^{2\nu} b^2 \sim N^{2\nu}, \quad \nu = 1/2,$$
 (1.5)

*i.e.*, despite the introduction of correlations, the polymer obeys random walk statistics.

The universal property just described becomes extremely handy in theoretical studies of chains by constraining them to a lattice. This constraint is an example of a nonuniform distribution of  $\theta$ . Both analytical calculations and simulations benefit tremendously from this simplification. The partition function becomes Gaussian, and the simulation database is much easily maintained and scanned. Visual examples of off- and on-lattice two-dimensional chains are given in Fig. 1.1. For large enough N it is almost impossible to distinguish between the two only by looking. Nevertheless, the lattice-constrained polymer swells to a larger extent by a constant prefactor because of the renormalization of link lengths due to this constraint.

In studies of semiflexible polymers, *i.e.*, chains which are not fully flexible as ideal chains but not as stiff as a rod, the term persistence length,  $l_{\rm p}$ , is often used rather than the Kuhn length, although both terms have practically the same meaning,  $l_{\rm p} = \kappa/(k_{\rm B}T) = b/2$ , where  $\kappa$  is the bending rigidity. Typical persistence lengths of polymers may range from a few nanometers to millimeters. For example, the persistence lengths of single-stranded DNA, double-stranded DNA, F-actin, and microtubule are 4nm, 50nm, 10 $\mu$ m, and 1-5mm, respectively ([7, 8, 9, 10], respectively).



Figure 1.1: Typical conformations of two-dimensional ideal chains obtained by simulations. Both chains are  $1.5 \times 10^6$  monomers long. The one on the right is constrained to a square lattice while the chain on the left is off-lattice with a uniform distribution of inter-link angle  $\theta$ .

## 1.1.3 Self-Avoidance, Flory Argument, and the Critical Dimension

As a second step in understanding polymers one wishes to consider self-avoidance, *i.e.*, excluded volume interactions, since two monomers sterically repel each other and cannot occupy the same position at a given time. A simplified tool to understand the effect imposed by such a restriction is the Flory argument [4, 11], which goes as follows: the relevant terms in the free energy of the system are written down (leaving prefactors out), and the energy is then minimized with respect to R to obtain the swelling exponent. For example, the free energy of a self-avoiding polymer is,

$$F = F_{\rm el} + F_v,$$
  
$$F_{\rm el} \sim k_{\rm B} T R^2 / (N l^2), \quad F_v \sim k_{\rm B} T v N^2 / R^d.$$
 (1.6)

The first term is related to stretching an ideal chain [the entropic spring derived in Eq. (1.3)]. The second term takes into account the exclusion of a monomer from a volume v around another monomer. The number of exclusions is proportional to the number of monomers N times their density  $N/R^d$ , where d is the embedding space dimension. Minimizing F with respect to R yields,

$$R \sim (vl^2)^{1/(d+2)} N^{\nu}, \quad \nu = 3/(d+2),$$
 (1.7)

*i.e.*,  $\nu = 3/4$  and 3/5 for two- and three-dimensional self-avoiding polymers, respectively.

As stated above, the Flory argument is not rigorous, and it is essential to confirm its results in another manner. The d = 2 case was solved exactly by Nienhuis [12] resulting in  $\nu = 3/4$  as obtained by Flory. For three-dimensional chains, numerical calculations and Monte Carlo simulations yield  $\nu \simeq 0.588$  [13, 14, 15]. This result, although close to the Flory prediction of 3/5, shows that it is inaccurate. The Flory argument is known to break in several other cases, for example, in the case of polyelectrolytes (charged polymer chains) [16]. Attempts to systematically improve the Flory argument have usually led to worse results. (See a detailed discussion of this issue in [4, 17].)

For a polymer residing in a four-dimensional space, Eq. (1.7) yields  $\nu = 1/2$ , which is the swelling exponent of an ideal chain. For  $d \ge 4$  self-avoidance ceases to influence the large-scale polymer statistics, and the chain behaves as an ideal chain. One may imagine that the monomers become so sparse in space that their interaction is negligible. For d > 4 the excluded-volume contribution to the free energy  $[F_v$  in Eq. (1.6)] becomes negligibly small and should be omitted from the equation. The dimension  $d_c = 4$  is called the critical dimension. In agreement with the theory of critical phenomena, for  $d > d_c$  all critical exponents get the values of the mean-field universality class [5].

## **1.1.4** Fractal Nature of Polymers

A fractal is a mathematical definition of an object which displays self-similarity, that is, an object that has the same shape as one or more of its subparts. A consequence of this characteristic is the scale-invariance of fractals [18]. To say it in simple words, no matter how much you "zoom" on this object, you will always see the same pattern. A trivial example of a fractal is a straight (infinite) line. When you "zoom in" and look at a part of it, you see exactly what was revealed with no magnification. Although fractals are not the focus of this thesis, polymers and manifolds show self-similarity characteristics (as will be shown below). To learn more about the nature of these objects we will examine a famous fractal—the Koch snowflake. Building it one starts with an equilateral triangle and replace the middle third of each side with a (smaller) equilateral triangle, as depicted in the upper part of Fig. 1.2. Repeating this process indefinitely yields the Koch snowflake. (See Fig. 1.2.)

To relate the mass (or "amount of curve") to the geometrical size of the object the fractal dimension is defined as  $\mathcal{D} = \log M_r / \log Z_r$ , where  $M_r$  is the ratio of the masses of the viewed object prior to and after zooming by a factor of  $Z_r$ .<sup>2</sup> For example, in Fig. 1.3 zooming (out) by a factor of 3 (from the small circle to the big one), the mass of the object in frame is increased by a factor of 4 and, thus, the fractal dimension of a Koch curve is  $\mathcal{D} = \log 4 / \log 3 \simeq 1.26$ . For the simple straight line example, zooming by a factor of  $Z_r$  increases the length of the viewed line by the same factor, and thus the fractal dimension of a straight line is  $\mathcal{D} = 1$ . Although mathematically the fractal dimension can be any non-negative number, for physically relevant objects  $\mathcal{D} \ge 1$ . Its upper limit is the dimensionality of the embedding space d. The relation  $\mathcal{D} = d$  is fulfilled for *compact* objects, *i.e.*, for objects that fill space—zooming out by a factor of  $Z_r$  will reveal a similar object,  $(Z_r)^d$ -times heavier. Nevertheless, we will see in the next section (1.2.2) that phantom, *i.e.*, unphysical, manifolds in d = 3 can have  $\mathcal{D} > d$ .

 $<sup>^{2}\</sup>mathcal{D}$  is sometimes referred to as the Hausdorff dimension.



Figure 1.2: Koch snowflake fractal. The upper part depicts the basic step in creating this fractal, *i.e.*, replacing the middle third of a section with an equilateral triangle. Middle drawing shows, from left to right, the shapes at different steps of the construction. The bottom drawing is a part of the Koch fractal, called sometime the Koch curve, which demonstrates clearly the self-similarity.

Polymers are not exactly self-similar in the sense that, when you zoom on them they do not look exactly the same. Nevertheless, their *statistics* show fractal characteristics. This is termed a statistical or random fractal [1, 18]. Multiplying the number of monomers N, and hence the polymer mass, by a factor of  $M_r$  leads to a mean end-toend distance  $R \sim (M_r N)^{\nu}$ . According to the definition of the fractal dimension, we get for a polymer  $\mathcal{D} = 1/\nu$ . A visual example of the self-similarity of an ideal chain is presented in Fig. 1.4.

## 1.1.5 Stretched Polymers and Blob Analysis

As a consequence of the analogy between polymer statistics and critical phenomena, small perturbation of a polymer chain may be studied using a scaling analysis [4]. To understand the concept of this theory in polymer physics let us consider the stretching of a chain by a fixed force  $\mathbf{f}$ , that is, holding both ends of the polymer and pulling them by a force  $\mathbf{f}$  one from the other. The statistical mechanics of such a system may be solved analytically in the case of ideal chains by simply calculating the partition



Figure 1.3: Calculating the fractal dimension of a Koch curve. Tripling the diameter of the circle or, alternatively, zooming out by a factor of 3, reveals a curve 4 times heavier. This leads to a fractal dimension  $\mathcal{D} = \log 4/\log 3$ .

function of the polymer (see, e.g., Eq. (A.1) for a chain in 2D). However, here we will focus on the qualitative behavior of such a system, which can be generalized to more complicated cases.

Scaling analysis suggests that the perturbation leads to a characteristic length scale  $\xi \sim k_{\rm B}T/f$ . For distances smaller than  $\xi$  the system is not affected by the perturbation, while for distances larger than  $\xi$ , the system behavior *is* modified. To say it differently, one can conceptually divide the chain into so-called Pincus blobs [19] of linear size  $\xi$ , see Fig. 1.5. It is an assumption of the blob analysis that the chain within the blob is unaffected by the perturbation, and thus the typical number of monomers within the blob g is given by  $\xi \sim g^{\nu}$ , where  $\nu$  is the swelling exponent of the unperturbed chain. For simplicity, we take hereafter the link length to be  $l \equiv 1$ . The pulling affects only the alignment of the blobs with respect to one another (the effective links that connect the blobs) in the direction of  $\mathbf{f}$ . Hence, the end-to-end distance follows the relation  $R \sim \xi N/g$ . Since one degree of freedom per blob has been restricted, the system pays a free energy penalty  $k_{\rm B}T$  per blob.

Solving the set of four relations,

$$\xi \sim g^{\nu}, \quad R \sim \xi N/g, \quad F \sim k_{\rm B} T N/g, \quad F \sim f R,$$
(1.8)



Figure 1.4: An ideal two-dimensional chain composed of  $10^6$  monomers (leftmost frame) displaying self similarity.



Figure 1.5: An ideal chain stretched by a constant force  $\mathbf{f}$ . The chain may be described by a set of blobs, where the chain within a blob is not disturbed while the blobs themselves are stretched with respect to one another.

leads to the following scaling laws:

$$R \sim N\left(\frac{f}{k_{\rm B}T}\right)^{(1-\nu)/\nu},$$
 (1.9)

$$g \sim (k_{\rm B}T/f)^{1/\nu}.$$
 (1.10)

This analysis breaks down for sufficiently small pulling force f, when the whole chain is contained in a single blob, that is, when the number of monomers within a blob is  $g \sim N$ , which is obtained for  $f \sim k_{\rm B}T/N^{\nu}$ . Substituting this value in Eq. (1.9) reveals the expected relation for an unperturbed chain,  $R \sim N^{\nu}$ . Below this limit, the force is too weak to perturb the chain. In the upper limit of the theory the chain breaks up into N blobs, or alternatively  $g \sim 1$ . This leads to  $f \sim k_{\rm B}T$  and a stretched statistics,  $R \sim N$ .

## **1.1.6** Monte Carlo Simulations of Polymers

In order to verify analytical results, or when calculation cannot be performed, it is beneficial to use computer simulations. The most common method in equilibrium statistical physics is the Monte Carlo simulation [20, 21, 22], which is mostly used with the Metropolis criterion [23] to perform a correct sampling of the configuration space. In a typical simulation, one builds up an initial configuration, and then a series of configurational changes are randomly generated (steps). Each step is accepted or rejected according to the Metropolis criterion [23]— if the system's energy decreases, or if the energy difference  $\Delta E$  obeys  $\exp[-\Delta E/(k_{\rm B}T)] > w$ , where w is a random number in the range [0,1] the step is accepted. After a sufficient number of steps the system relaxes to its equilibrium state. It is the Metropolis criterion which takes care of correct sampling by weighing each configuration with its Boltzmann probability. In order to capture the equilibrium characteristics correctly it is important to average over uncorrelated measurements, either by starting from different initial configurations or, alternatively, by running a number of steps much greater than the one needed for relaxation. Another comment is that a Monte Carlo simulation does not represent the real dynamic behavior of the system, and the number of steps taken is not necessarily proportional to real time.

#### Monte Carlo Models of Polymers

A common off-lattice method to simulate polymer statistics is the rigid-links model [21], which considers the polymer links to be of fixed length. In a possible Monte Carlo step a monomer is repositioned, but since it is attached to two other monomers by rigid rods of length l, its new position is limited to the perimeter of a circle on the midplane between its two neighbors. (For a polymer confined to 2D, this circle turns into just two possible positions as can be seen in Fig. 3.4.) As a consequence of this rigidity and due to the small configurational space available at each Monte Carlo step, simulations become inefficient, and the number of steps needed to reach relaxation, or alternatively, to produce an uncorrelated configuration, is relatively high. Another

possible step is the repositioning of a whole section of the polymer between monomers i and j, simply by rotating this section around the axis that connects monomers i and j. This is sometime referred to as a pivot step [24].

A different model is the bead-and-tether one [21], where the monomers are represented by beads of radius a and the links by tethers with a maximum length l, *i.e.*, link lengths are not fixed. The simplest potential between monomers i and j describing this model is

$$V_{ij} = \begin{cases} 0 & 2a < r_{ij} < l \\ \infty & \text{elsewhere,} \end{cases}$$
(1.11)

where  $r_{ij}$  is the intermonomer distance. A possible Monte Carlo step is to move a randomly chosen node by some displacement in an arbitrary direction. The absence of the rigidity constraint allows this model to reach the equilibrium state in a substantially smaller number of steps. Another feature of this model is the ability to impose self-avoidance, by setting a > 0. (See, *e.g.*, Ref. [25].)

Two other common models are the lattice-constrained polymer (which was briefly mentioned above) and the bead-and-spring model, where harmonic springs are used instead of tethers of maximum length. (See more on these models in [21].) Extending any of these simulations to take into account polymer semiflexibility is rather simply achieved by summing over all adjacent links the energy term  $\kappa \sum (1 - \hat{\mathbf{l}}_i \cdot \hat{\mathbf{l}}_{i+1})$ , where  $\hat{\mathbf{l}}_i$  is a unit vector in the direction of link *i* and  $\kappa$  is the polymer bending rigidity. (In this thesis, however, bending rigidity will not be explicitly considered.)

#### **Behavior Near Continuous Transitions**

For systems near a critical point the correlation length becomes very large. Using simple Monte Carlo steps of local displacements, it becomes almost impossible to "escape" to the next uncorrelated configuration. This is called *critical slowing down* of the simulation [21, 22]. In order to overcome such a difficulty it is important to perform collective steps, for example, making several simple steps before applying the Metropolis criterion. Another example is the pivot step suggested above for the rigid-rod model.

A real phase transition occurs only in the thermodynamic limit, *i.e.*, for an infinitely large system. Simulations, however, are performed on finite-size systems. Thus for continuous transitions the correlation length  $\xi \sim t^{\nu}$ , t being the control parameter, cannot exceed the system size L. As a consequence, the order parameter and the compressibility, instead of obeying the simple power laws  $M \sim |t|^{-\beta}$  and  $\chi \sim |t|^{\gamma}$ follow the finite-size scaling laws [26],

$$M \sim L^{-\beta/\nu} \tilde{M}(L^{1/\nu}|t|),$$
 (1.12)

$$\chi \sim L^{\gamma/\nu} \tilde{\chi}(L^{1/\nu}|t|), \qquad (1.13)$$

where  $\tilde{M}$  and  $\tilde{\chi}$  are universal functions.

## 1.1.7 Two-Dimensional Polymeric Rings

In the context of this thesis, polymer rings constrained to a plane are a simplified, somewhat artificial case of random manifolds. The reduced dimensionality makes the calculation more tractable and in several cases the statistical mechanics of such systems may be solved analytically. Even such simplified objects exhibit a variety of shapes and shape transformations, as will be seen in Chapter 3.

Nevertheless, treating such rings is not purely academic. Polymeric rings exist in nature, for example, the denaturation of a section in the double stranded DNA forms a ring (DNA bubble), composed of single stranded DNA [27]. These rings may be constrained to two-dimensions, either by making them adsorb on a surface or by trapping them at the interface between two phases. For example, single-wall carbon nanotubes can be deposited in a ring shape on hydrophilic surfaces as part of a nanodevice [28], and DNA plasmids were deposited on mica surfaces to reveal a swelling exponent of  $\nu = 3/4$  [29], as expected for self-avoiding polymers D = 2. Experiments of polymer rings which are relevant to this thesis (Chapters 3 and 4) were conducted by Rabe and coworkers [30]. In these studies, DNA plasmids were embedded in an ultrathin liquid film. The conformations of unperturbed rings appear crumpled but when imaged by scanning force microscopy (SFM) in a tapping mode, the rings swell into smooth 2D bubbles. It is believed that the SFM tapping exerts pressure on the liquid film which causes this inflation.

## **1.2** Membranes and Vesicles

Biological membranes are complex structures, composed mainly of a lipid bilayer, but also of proteins and sterols. The lipid molecules, forming the bilayer, are amphipathic, that is, they contain both a hydrophilic (water soluble) headgroup, which is either polar or charged, and a hydrophobic (water insoluble) tail, composed of fatty acids. Their self-assembly into a bilayer is one of the many possible phases they form in aqueous solution [31, 32]. The other components of the membrane are either hydrophobic or contain a hydrophobic region which, is buried in the core of the membrane. Note that the membrane as an object is stabilized only by weak forces due to the hydrophobic effect rather than covalent bonds.

Small enclosures, of up to tens of microns in diameter, bounded by a lipid bilayer are generally termed *vesicles*. (In some cases, but not throughout this work, this term is used to describe also objects enclosed by several membranes — a multilamellar vesicle.) Into this classification fall natural components—small organelles (*e.g.*, lysosomes), transport vesicles, and signal transmitters such as synaptic vesicles [33, 34], as well as artificially made liposomes, which are used, for example, in pharmaceutical and cosmetic applications [35]. The size of artificial vesicles may range from a few tens of nanometers to tens of microns in diameter, depending mainly on the preparation method [36].

A membranal envelope is an essential feature for the existence and functionality of all living cells and their internal organelles. The outer membrane of the cell is referred to as the plasma membrane and is composed mainly of phospholipids. One of its many roles is to regulate transport of molecules into or out of the cell. Due to its hydrophobic core, small non-ionic molecules can permeate and diffuse through the membrane, while the translocation of larger or ionic ones depends on protein mediation, such as ion channels. Water, for example, are polar, and thus their permeation rate is slow compared to molecular time but still physically relevant (of order  $10^{-5}-10^{-4}$  s per molecule for a bare lipid bilayer [37]). Another relevant biological membrane is that of the nucleus, which is filled with nuclear pore complexes [38]. This huge proteinic channel has a diameter of  $\simeq$  50nm and allows the free diffusion of small molecules (up to 40 kDa) into and out of the nucleus, while the transport of larger molecule such as proteins and mRNA is regulated [38]. Essentially, the nuclear membrane functions in a similar manner to the plasma one, allowing some of the molecules to permeate freely and hindering the permeation of others.

In this thesis and in similar theoretical studies, however, the whole envelope is in frame and the membrane is described using coarse-grained parameters such as bending rigidity, the total area of the envelope, pressure difference across the two faces and so on. The characteristics of individual components of the membrane are only implicitly included in the phenomenological parameters of the membrane itself. As an illustration, for example, the bending rigidity of a single-component membrane depends on the molecular length of the hydrophobic tail  $n_{\rm C}$  (alkyl carbon number) as  $\kappa \sim n_{C}^{P_{\rm C}}$ , where  $P_{\rm C} \simeq 3$  [39, 40]. Another example is the incorporating cholesterol molecules into the hydrophobic core, which increases the bending rigidity by up to a factor of 3 [41, 42] and reduces the membrane fluidity [36]. More relevant to this thesis is the membrane permeability to various solutes, which increases with the concentration of unsaturated phospholipids in the membrane [36]. Permeation of water molecules can also be dramatically increased by incorporating proteinic water channels named Aquaporins [43, 44].

Two interesting features of vesicles arise from the semipermeability of their membranes. The first is that the vesicle volume is not fixed due to the permeation of solvent molecules in and out of the vesicle. The second stems from the fact that large molecules cannot escape the envelope of the vesicle and thus lead to osmotic swelling. We call such a system a *particle-encapsulating vesicle*.

Concentration differences across biological membranes, which are manifest in pressure and/or voltage differentials, are essential for the activity and vitality of the cell by providing a driving force for Adenosine triphosphate (ATP) synthesis, reception of outer signals, expulsion of waste and so on [34]. Furthermore, pressure gradients affect the shape of the cell. Concentration differences are maintained by proteinic pumps and are energy-consuming [34].

#### **1.2.1** Smooth Membranes and the Helfrich Hamiltonian

The membrane encapsulating a cell or vesicle is only two molecules thick (about 4nm) while its lateral size may be of the order of microns. Having the whole cell in frame,

the membrane is tremendously thin and may be represented by a two-dimensional surface. Such a surface has two internal coordinates,  $t_1$  and  $t_2$ , and its conformation is characterized by the spatial function  $\mathbf{R}(t_1, t_2)$ . This function defines two principal (normal) curvatures,  $c_1$  and  $c_2$  (which are the smallest and largest local curvatures, see *e.g.*, Refs. [45, 46]).

For a vesicle whose energy is dominated by the bending energy, one may write the free energy as an integral over the whole vesicle surface,

$$F = \oint dA \left[ \frac{\kappa}{2} \left( \frac{c_1 + c_2}{2} - c_0 \right)^2 + \kappa_{\rm G} c_1 c_2 \right], \qquad (1.14)$$

where  $\kappa$  and  $\kappa_{\rm G}$  are the bending modulus and Gaussian modulus, respectively, and  $c_0$  is the spontaneous curvature, which vanishes if the two faces of the bilayer are symmetrical. (The two can differ, for example, due to a different composition or integral proteins, which cause a distortion on one leaflet.) Although a simpler form of the free energy with  $\kappa_{\rm G} = 0$  and  $c_0 = 0$  had been used a few years earlier by Canham [47], the formalism of Eq. (1.14) was first devised by Helfrich [48] and is termed either the Helfrich or Canham-Evans-Helfrich Hamiltonian.

While the bending rigidity  $\kappa$  of polymers is measured in units of length times energy, and thus leads to a typical length scale,  $l_{\rm p} = \kappa/(k_{\rm B}T)$  (see Section 1.1.2), the one for surfaces has units of energy, and the Helfrich Hamiltonian is scale-invariant. Nevertheless, taking into consideration a molecular cutoff a, comparable to the membrane thickness (a few nm), leads to a persistence length  $l_{\rm p} \sim a \exp[2\pi\kappa/(k_{\rm B}T)]$  [49, 9]. Typical values of  $\kappa$  for a bilayer membrane is between a few  $k_{\rm B}T$  to tens of  $k_{\rm B}T$ , which leads to a persistence length ranging between a micron and tens of meters and even more.

According to the Gauss-Bonnet theorem, the integration over the second term in Eq. (1.14) yields  $\oint dAc_1c_2 = 4\pi(1-G)$ , where G is the genus of the surface, *i.e.*, the number of handles [45, 46]. For vesicles which do not change their topology, this term is constant and is thus omitted in many theoretical works. Nevertheless, if one studies surfaces with a changing topology, such as cell splitting, budding or phagocytosis, this term must be taken into account.

For a given volume-to-surface-area ratio  $v = V/A^{3/2}$ , minimizing Eq. (1.14) with

respect to the contour of the vesicle (*e.g.*, by solving the corresponding Euler-Lagrange equations while assuming axisymmetry), yields the most probable shape. This simple form of the free energy gives rise to a variety of shapes (stomatocyte, oblate, and prolate) and to transitions between them [50]. Since the bending rigidity is a prefactor of the Hamiltonian it does not affect the most probable configuration and enters only when vesicle fluctuations are considered. Those studies, however, address the case where the lateral size of the vesicle, L, is much smaller than the persistence length,  $l_p$ , and so thermal fluctuations around this minimum energy state are small.

Simple improvement to this minimalistic model is achieved by adding terms to the Helfrich Hamiltonian. For example, terms which take into account the area difference between the two layers in the bilayer give rise to a pear shape as well as a budding transition (see, *e.g.*, Ref. [51]). Other possible improvements are taking into account the inhomogeneity of the system, *e.g.*, taking a nonuniform spontaneous curvature, or considering non-axisymmetric shapes (*e.g.*, Ref. [52]).

#### Pressurized Vesicles

Since vesicles are almost always immersed in a solution which includes large molecules or particles that cannot permeate the membrane, a more realistic approach to characterize the behavior of vesicles is achieved by introducing another term, pV, to the Helfrich Hamiltonian, where p is the pressure difference between the interior and exterior of the envelope. To be more specific, and using a simple ideal solution description, one may write  $p = k_{\rm B}T(Q/V - c)$ , where Q is the number of particles trapped in the vesicle, and c is the concentration of particles in the embedding solution (outside the vesicle).

First, let us note, that this pressure difference term leads to another characteristic length,  $L_p = |k_{\rm B}T/p|^{1/d}$ , where d is the embedding dimension [25, 76]. Vesicles with  $L \gg L_p$  are crumpled and random, while those with  $L \ll L_p$  are smooth due to the pressure difference. Recall that bending rigidity causes smoothness for  $L \ll l_p$ . For real vesicles, *i.e.*, for relevant values of  $\kappa \sim 10k_{\rm B}T$  and  $L \sim 1\mu$ m, the energy related with the term pV exceeds that of the bending rigidity  $\kappa$  for concentration differences as small as  $10^{-7}$ M, which is orders of magnitude smaller than the concentration of typical solutions. As a result, when the free energy of the vesicle is minimized with respect to the its volume, V,  $\kappa$  plays a negligible role, and the volume is selected such that the pressure difference is practically zero. For an ideal solution this is obtained for V = Q/c. Thus, the vesicle adjusts its volume through water permeation in order to achieve a vanishingly small pressure difference.

## **1.2.2** The Fractal Nature of Manifolds

Using the perspective discussed in Section 1.1.4 one may refer to random surfaces as statistical fractal objects. Studies regarding properties of random manifolds, usually discretize the surface and consider a set of nodes connected by tethers (*e.g.*, Ref. [53]), or alternatively, a set of plaquettes, attached to one another (see [54]). However, it was shown that the swelling exponent of these objects depends on the manner one constructs them. For example, for a given topology the radius of gyration of a phantom surface (*i.e.*, without self-avoidance), obeys

$$R_{\rm g}^{\ 2} \sim \log(L),\tag{1.15}$$

where L is the lateral size of the surface [55, 56, 57, 58]. Since this scaling is weaker than a power law the fractal dimension is  $\mathcal{D} \to \infty$ . On the other hand, if the surface is constructed by adding plaquettes at a given chemical potential, one gets a finite fractal dimension which depends on the connectivity of the surface [54].

Before continuing, we note that the simple relation between  $\nu$  and  $\mathcal{D}$  presented for polymers in Section 1.1.4 can be generalized to *D*-dimensional manifolds as follows: the radius of gyration is related to the lateral size of the manifold by  $R_{\rm g} \sim L^{\nu}$ , while the fractal dimension is related to the mass of the manifold (which is proportional to  $L^D$ ) by  $R_{\rm g}^{\ \mathcal{D}} \sim L^D$ . Thus, for a general *D*-dimensional manifold one has  $\mathcal{D} = D/\nu$ .

The anomaly of phantom surfaces with a diverging fractal dimension is removed when the bending rigidity  $\kappa$  increases beyond a critical value  $\kappa_c \simeq k_B T/3$ , where the surface undergoes a continuous transition into smooth statistics with  $R_g \sim L$ . This transition is referred to as the crumpling transition [57, 58]. <sup>3</sup> Alternatively, the phantom manifold anomaly is removed when self-avoidance is introduced. A simple Flory argument as in the case of polymers (see Section 1.1.3) gives a qualitatively

<sup>&</sup>lt;sup>3</sup>We will see along this thesis, that smoothening of closed random surfaces can also be achieved by swelling, *i.e.*, the introduction of an inflating pressure difference

correct picture [59]. In such an approach, the free energy of the manifold is given by

$$F = F_{\rm el} + F_v,$$
  
 $F_{\rm el} \sim k_{\rm B} T R^2 L^{D-2}, \quad F_v \sim k_{\rm B} T v L^{2D} / R^d,$  (1.16)

where, again,  $F_{\rm el}$  is the energy related with stretching a Gaussian manifold to a lateral distance R, and the second term is proportional to the number of exclusion interactions, with v being the excluded volume. Minimizing Eq. (1.16) with respect to R, one gets,

$$R \sim L^{\nu}, \quad \nu = (D+2)/(d+2),$$
 (1.17)

and thus a fractal dimension  $\mathcal{D} = D(d+2)/(D+2)$ . For a polymer, D = 1 and the swelling exponent coincides with the one already found in Eq. (1.7). For a twodimensional surface embedded in d = 3, this prediction yields  $\nu = 4/5$ , which was verified by Monte Carlo simulations of fixed-connectivity triangulated surfaces as explained below [53, 60].

#### **1.2.3** Monte Carlo Simulations of Surfaces

The bead-and-tether model presented for polymers in Section 1.1.6 is easily extended to the case of two-dimensional manifolds by considering a triangulated tethered surface (e.g., Ref. [53]) with a given topology (connectivity). A visual example is presented in Fig. 1.6. This model is sometimes referred to as a polymerized membrane. The logarithmic collapse of phantom manifolds, Eq. (1.15), was verified using simulations of such a model. Self-avoidance is easily introduced using the same potential used for polymers, Eq. (1.11), and a proper choice of a, l, and the maximum step size. Such a treatment leads to a swelling exponent similar to that obtained by the Flory argument, Eq. (1.17). (See further discussion of this issue in Ref. [60].)

However, due to the fixed-connectivity constraint, these Monte Carlo simulations cannot capture correctly the ensemble of all surfaces with a given surface area. A vivid example of this deficiency arises when one imagines a glove. It is possible to move its palm and fingers, deflate them, and even turn a right-hand glove into a left-hand one, but due to the original shape it would never turn into a sphere! Such a transformation requires relaxation of local strains, *i.e.*, fluidity. Fluidity can be introduced to Monte



Figure 1.6: A triangulated tethered surface. The figure on the right depicts the topology (connectivity) of the (flattened) surface, while the one on the left is a typical crumpled conformation. Figure taken from Ref. [53].

Carlo simulations by allowing vertices to move on the surface. One way is to randomly break a 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). See illustration in Fig. 5.1. This scheme was first introduced by Kazakov *et al.* [61]. For a self avoiding random manifold, the fluidity scheme leads to deflation of the surface, such that it behaves like a self-avoiding branched polymer [62, 63]. After such fluidity is introduced the set of configurations is presumed to capture all possible conformations of a fluid surface having a given maximum area. We will use this scheme in Chapter 5 to simulate the behavior of three-dimensional fluid vesicles.

#### Surfaces Constrained to a Lattice

In a similar manner to polymers, surfaces can also be constrained to a lattice, which in most studies is a cubic one. In such a representation a surface is a set of square plaquettes, *i.e.*, faces of the elementary cells, where each edge on the surface is shared by exactly two plaquettes. Using this representation one can investigate the statistics of fixed-connectivity surfaces as well as random-connectivity ones. In the case of selfavoiding random connectivity, the branched-polymer-like behavior mentioned above is obtained (*e.g.*, Ref. [64]). Finally, let us mention a curious distinction between the simulations of on- and off-lattice rings and vesicles. We have seen in Section 1.1.2 that the overall statistics of polymers is not affected by constraining them to a lattice (see also Fig. 1.1). Nevertheless, while a fully swollen off-lattice two-dimensional ring attains a circular shape, a similar ring constrained to a lattice will become square. The same occurs for three-dimensional vesicles, *i.e.*, an off-lattice swollen vesicle becomes spherical, while a lattice-constrained one swells into a cube [65, 66]. Thus, since a high degree of swelling suppresses the fluctuations of a random closed manifold, the equivalence of off- and on-lattice models eventually breaks down.

#### **Coarse-Grained Model of Membranes and Vesicles**

The artificial representation of surfaces presented above addresses a statistical mechanical system rather than a biologicaly relevant one. There are, however, other simulation techniques which address the behavior of real membranes. One of them is molecular dynamics, in which all the atoms within a system (including those of the solvent molecules) are represented and are allowed to interact with one another [67, 68]. Obviously such a simulation requires strong computing power. Current technological advances allow simulations of small membranal systems, consisting of a few hundreds of amphiphiles, and can simulate a limited time scale, which does not exceed microseconds [68]. Another simulation technique is the coarse-grained models, in which the building blocks of the membrane, *i.e.*, the surfactants, are represented by 3 to 5 monomers, thus reducing the number of interacting particles by two orders of magnitude. These models, although less realistic, provide a more efficient simulation methodology for large membranes (a few thousands of amphiphiles) [69].

## **1.3** Thesis Overview

We have seen above two approaches to address the behavior of surfaces. The first (Section 1.2.1) uses the Helfrich Hamiltonian and considers smooth surfaces. This description holds in the regime of low temperature, where the lateral size of the surface is much smaller than the persistence lengths arising from bending rigidity and pressure difference,  $L \ll l_p, L_p$ . The second approach (Section 1.2.2) depicts the surface as a

fractal random manifold and aims at the high temperature regime,  $L \gg l_p$ ,  $L_p$ . In this thesis we will mainly focus on the second description of random surfaces, investigating how such strongly fluctuating envelopes respond to a pressure difference or the effective osmotic pressure exerted by trapped particles.

We start in Chapter 2 with a general scaling analysis for the swelling of closed random manifolds. Two scenarios are considered — that of pressurized vesicles and that of particle-encapsulating ones. The resulting scaling laws are then verified in three model systems: two-dimensional, freely jointed and self-avoiding rings (Chapters 3 and 4), and a three-dimensional self-avoiding fluid vesicle (Chapter 5). In Chapter 6 we aim at the more realistic, low temperature regime and study the behavior of highly swollen particle-encapsulating vesicles immersed in a solution of given concentration. Finally, all the results are summarized and discussed in Chapter 7.

# Chapter 2

# Scaling of Swollen Closed Random Manifolds

In this chapter we present general scaling analyses for the swelling of closed random manifolds subject to either a fixed pressure difference or a fixed number of trapped particles. It is shown that the two swelling scenarios are not always thermodynamically equivalent. While in the first scenario the swelling may exhibit a criticality, the swelling of particleencapsulating random manifolds is gradual with the number of trapped particles. The resulting scaling laws serve as guidelines for the rest of the thesis.<sup>1</sup>

## 2.1 Introduction

As has been presented in Chapter 1, there has been considerable interest in the past few decades in the statistical mechanics of membranes and surfaces [71]. This has been partly motivated by the ubiquity of bilayer membrane vesicles [72] in various natural and industrial systems. The lateral dimension L of these envelopes is much larger than their thickness and, therefore, they can be treated to a good approximation as purely (d-1)-dimensional objects, where d is the embedding dimension. Another consequence of the small thickness is that the membrane resists stretching much stronger than bending. Hence, the surface area of the manifold is usually taken as fixed. The statistical mechanics of such a manifold involves an interplay between conformational fluctuations and bending elasticity, leading to a characteristic persistence length,  $l_p$ 

<sup>&</sup>lt;sup>1</sup>The results presented in this chapter were published in Ref. [70].

 $[49]^2$  — 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  $l_p$  but also by its 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 surface area A. One body of works, *e.g.*, Refs. [51, 47, 48, 50], considered 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 d = 3. The various equilibrium shapes are derived as ground states of the elastic Helfrich Hamiltonian (see Section 1.2.1), which depend on the dimensionless volumeto-area ratio,  $V/A^{3/2}$ . Another body of works considered the ensemble of fixed pressure difference p across the manifold. These include Gaussian [75] freely jointed [76] and self-avoiding rings [25, 73, 74] in d = 2, as well as model fluid vesicles in d = 3[77, 78, 79, 80, 81, 59, 82, 65]. Most works assumed the random, high-temperature limit ( $l_p \ll L$ ), yet the crossover to  $l_p > L$  was addressed as well [25, 76, 80, 81, 59].

As far as equilibrium averages are concerned, the ensembles of fixed V and fixed p are equivalent, *i.e.*, related via 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-encapsulating vesicles is not only academic, since most actual vesicles are immersed in solution and their membrane, over sufficiently long time, is semipermeable, allowing solvent to permeate while keeping the solute trapped inside [83, 84]. (See Section 1.2 and Chapter 6.) Knowing the particle number Q does not imply, a priori, a certain osmotic pressure, because the manifold is free to select its mean volume and, thus, the mean concentration. Since the mean volume and pressure should monotonously increase with Q, one expects to establish equivalence between this fixed-Q ensemble and the other two. However, we will show along this thesis that this is not always true.

In this chapter we present a general scaling analysis in order to create a unified description for a (d-1)-dimensional random manifold in d dimensions swollen by

<sup>&</sup>lt;sup>2</sup>See also Section 1.2.1.

either a fixed pressure or a fixed number of trapped particles. We thereby clarify when these two ensembles are inequivalent. In the following chapters (Chapters 3–5) we will check this unified description in detail in several model systems.

## 2.2 Scaling Analysis

We begin our investigation performing a general scaling analysis [4, 73] for a closed (d-1)-dimensional random manifold, composed of N nodes and embedded in d dimensions. A schematic representation of the system is given in Fig. 2.1. In response to perturbation (pressure difference p or Q trapped particles), the system 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  $k_{\rm B}T \equiv 1$  (Section 1.1.5),

$$\sigma \xi^{d-1} \sim k_{\rm B} T \equiv 1, \tag{2.1}$$

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

$$g^{\nu} \sim \xi^{d-1},\tag{2.2}$$

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,

$$R^{d-1} \sim \frac{N}{g} \xi^{d-1}.$$
 (2.3)

So far, the relations, Eqs. (2.1)–(2.3), have been independent of the nature of the perturbation (p or Q). The difference between the two swelling scenarios enters via the Laplace law, taking the following forms in the fixed-p and fixed-Q ensembles, respectively:

$$\sigma/R \sim p,$$
 (2.4a)

$$\sigma/R \sim Q/R^d$$
. (2.4b)



Figure 2.1: A schematic representation of a closed manifold subject to a fixed-p or fixed-Q perturbation. Due to the perturbation the manifold, containing a total of N nodes and having a radius of gyration R, can be divided into N/g subunits (blobs), each containing g nodes and having radius  $\xi$ .

Solving the set of relations for the fixed-p ensemble, Eqs. (2.1)–(2.4a), one arrives at the following power laws:

$$\langle V \rangle \sim R^{d} \sim N^{d/(d-1)} (p^{d-1} N)^{d(1-\nu)/[(d-1)(d\nu-1)]},$$
  
 $\sigma \sim (p^{d-1} N)^{\nu/(d\nu-1)}.$  (2.5a)

(This result, in a slightly different form, has been already obtained in Ref. [77].) Two observations readily follow from Eq. (2.5a). First, the characteristic pressure difference required to appreciably swell the manifold scales as  $p \sim N^{-1/(d-1)}$  regardless of  $\nu$ . This characteristic value reflects the interplay between the mechanical work of swelling 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 and one expects criticality [73]. Both conclusions are borne out by previously studied models. The mean volume of Gaussian rings [75], having d = 2 and  $\nu = 1/2$ , (*i.e.*,  $d\nu = 1$ ,) diverges at a critical pressure  $p_c \sim N^{-1}$ . By contrast, self-avoiding rings, with d = 2and  $\nu = 3/4$ , swell gradually with p [25, 73].

Turning to the fixed-Q case, which is the focus of this study, and solving the

relations Eqs. (2.1)–(2.4b), we find the power laws,

$$\langle V \rangle \sim N^{d/(d-1)} (Q/N)^{d(1-\nu)/(d-1)},$$
  
 $\sigma \sim (Q/N)^{\nu}.$  (2.5b)

The two 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 here a vanishing external pressure.<sup>3</sup> 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, *i.e.*, no criticality. Both conclusions will be verified in Chapters 3–5.

The two blob analyses, along with the resulting power laws [Eqs. (2.5a) and (2.5b)], should hold so long as 1 < g < N. This corresponds to the restrictions,  $N^{-d\nu/(d-1)} and <math>1 < Q < N$ . At larger swelling, nonetheless, we expect smooth manifolds with  $\langle V \rangle \sim N^{d/(d-1)}$ . According to the Laplace law this leads to a surface tension  $\sigma \sim p N^{1/(d-1)}$  and  $\sigma \sim Q/N$ . Combining these large-swelling results with Eqs. (2.5a) and (2.5b), 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:

$$\langle V \rangle = N^{d/(d-1)} f_p(p N^{1/(d-1)}),$$
  
 $\sigma = h_p(p N^{1/(d-1)}),$  (2.6a)

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

$$\sigma = h_Q(Q/N).$$
(2.6b)

The scaling functions for the mean volume,  $f_p$  and  $f_Q$ , should cross over from the power laws of Eqs. (2.5a) and (2.5b) 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. (2.5a) and (2.5b) to linear ones. Equations (2.5) and (2.6) are the central predictions of the scaling theory, and will be verified

 $<sup>^{3}\</sup>mathrm{The}$  case of fixed number of encapsulated particles and fixed outer pressure will be addressed in Chapter 6.

for three model systems in the following chapters.

## 2.3 Discussion

The scaling analysis presented in Section 2.2 yields a unified account of the swelling of random manifolds with increasing pressure difference or number of encapsulated particles. Similar scaling analyses for the case of fixed p have been already presented in Refs. [73, 77]. Those analyses and ours coincide in the power-law regime, Eq. (2.5a). However, while the analyses of Refs. [73, 77] 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 including the highly swollen state. Thus, on the one hand, our scaling relations, Eqs. (2.6a) and (2.6b), cannot account for the unperturbed state and give a vanishing mean volume in the limit of vanishing perturbation. The range of p (or Q) where this deficiency is relevant vanishes, nonetheless, in the thermodynamic limit.<sup>4</sup> On the other hand, whereas the earlier analyses assumed that scaling broke down at sufficiently large swelling [73, 77], we claim that Eqs. (2.6a) and (2.6b) 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 will show in Chapters 3–5 that it does. Hence, provided that the swelling exhibits no criticality, the scaling relations Eqs. (2.6a) and (2.6b) will be shown to be applicable for a broad range of systems.

According to Eq. (2.5a) a criticality emerges in the fixed-p ensemble if  $d\nu = 1$ . This leads, according to Eq. (2.5b) for particle-encapsulating manifolds, to a linear dependence of  $\langle V \rangle$  on Q. Alternatively, for a general scaling behavior of particleencapsulating vesicles, which follows a power-law dependence,  $\langle V \rangle \sim Q^{\alpha}$ , changing variables to p = Q/V we get in the fixed-p ensemble that the mean volume follows  $\langle V \rangle \sim p^{\alpha/(1-\alpha)}$ , that is, a criticality emerges if  $\alpha = 1$ . We will see further on, in Chapters 3 and 5, model systems which exhibit this criticality. This point will be further clarified in Chapter 7.

According to the scaling analysis, to get a criticality during the swelling of pressurized vesicles one should consider objects with an unperturbed swelling exponent

<sup>&</sup>lt;sup>4</sup>The range in the fixed-*p* ensemble is  $pN^{1/(d-1)} < N^{(1-d\nu)/(d-1)}$ , which vanishes as  $N \to \infty$  for  $d\nu > 1$ , *i.e.*, so long as there is no criticality. In the fixed-*Q* case the range is Q/N < 1/N, which is irrelevant regardless of  $\nu$ .

 $\nu = 1/d$ . For objects embedded in d = 2,  $\nu = 1/2$  corresponds to Gaussian rings, and indeed, the mean area of such rings diverges at a critical pressure [75, 85, 86]. The same swelling exponent characterizes freely-jointed rings as well. It will be shown in Chapter 3 that the inflation of these objects undergoes a phase transition. However, if the blob analysis holds, this also implies that for  $d \ge 3$  criticality will emerge only when the fractal dimension of the objects is  $\mathcal{D} = D/\nu = (d-1)d$  (see Section 1.1.4 and Section 1.2.2), which is larger than the upper bound set by compact objects,  $\mathcal{D} = d$ . Obviously, such a scenario is physically impossible.

We have seen in these analyses that a criticality may appear during the swelling of pressurized vesicles, while for particle-encapsulating ones, the swelling is always gradual. These two ensembles, therefore, may be thermodynamically inequivalent. Practically, this analysis gives rise to inequivalence only for the single case of d = 2and  $\nu = 1/2$ . The rest of the cases, as far as this analysis goes, should not involve criticality and should be able to move from one representation to the other using a one-to-one smooth transform. Nonetheless, as will be shown in Chapter 5, there could be exceptional cases where the blob analysis is invalid, and a phase transition with increasing p appears in d = 3.
# Chapter 3

# Swelling of 2D Freely Jointed Rings

As a first example for the realization of the scaling analyses of Chapter 2 we study a two-dimensional model of a freely jointed ring. For this model, the scaling analyses predict criticality in the swelling with increasing pressure difference p and gradual swelling with increasing number Q of trapped particles. In this chapter we study both scenarios. For the fixed-p ensemble, inextensible chains of N monomers are considered. Using a Flory argument, mean-field calculation and Monte Carlo simulations, we show that at a critical pressure,  $p_{\rm c} \sim N^{-1}$ , the ring undergoes a second-order phase transition from a crumpled, random-walk state, where its mean area (twodimensional volume) scales as  $\langle V \rangle \sim N$ , to a smooth state with  $\langle V \rangle \sim N^2$ . The transition belongs to the mean-field universality class. At the critical point a new state of polymer statistics is found, in which  $\langle V \rangle \sim N^{3/2}$ . For  $p \gg p_{\rm c}$  we use the transfer-matrix technique to derive exact asymptotic expressions for the thermodynamic properties of the smooth state. For the fixed-Q scenario, both Gaussian and inextensible freely jointed rings are studied. The Gaussian model is solved exactly, and the freely jointed one is treated using a Flory argument, mean-field theory, and Monte Carlo simulations. In the two models the swelling is gradual with Q and no criticality is observed. In agreement with the scaling analysis, the mean volume follows a single scaling law in the fixed-Q case. By contrast, when the particles are in contact with a reservoir of fixed chemical potential, the

criticality of the fixed-p ensemble is retained.<sup>1</sup>

# 3.1 Introduction

Considerable theoretical efforts were directed during the 1980s and 1990s at random polymer rings constrained to a plane, both as a fundamental problem of statistical mechanics [89, 90, 91, 92, 93, 94] and as a highly idealized model for membrane vesicles [25, 73, 74, 75, 85, 86, 95, 96, 97]. The statistics of 2D chains have been studied also experimentally, using polymers adsorbed at liquid interfaces [98, 99] or membranes [100], as well as vibrated granular chains [101, 102] and rings [103, 104]. In those experimental systems both random-walk and self-avoiding-walk statistics were observed.

Pressurized 2D rings were theoretically investigated in a number of works [25, 73, 74, 75, 85, 86, 95, 96]. In the Rudnick-Gaspari model [75, 85, 86] the ring is represented by a closed Gaussian chain of N springs of fixed elastic constant, subject to an inflating pressure differential p. At a critical pressure  $p_c \sim N^{-1}$  the mean area was found to diverge (the ring inflates to infinity). This divergence, obviously, is made possible by the extensibility of the chain, *i.e.*, the ability of the springs in this model to be infinitely stretched. For these Gaussian chains the embedding dimension is d = 2and the swelling exponent is  $\nu = 1/2$ . Hence, the reported criticality is in line with the scaling analysis of the previous chapter, Eq. (2.5a). In addition, according to this analysis the criticality should be removed for particle-encapsulating vesicles — a prediction which we are going to check below. Two dimensional Gaussian rings are unique in the sense that both contributions to the free energy (stretching and pressure related one) are proportional to the mean-square link length. That is, any addition to the free energy which is not proportional to the mean-square link length will most probably remove this criticality.

In the current chapter we revisit the Rudnick-Gaspari model while imposing inextensibility of the chain as is actually appropriate for real polymers or vesicles. This

<sup>&</sup>lt;sup>1</sup>The results presented in this chapter were published in Refs. [87, 88]. Since this investigation of freely-jointed rings had been conducted long before the scaling analysis of Chapter 2 was devised, it is done in more mathematical detail than the investigations presented in the following chapters (Chapters 4 and 5).

constraint does not change the swelling exponent of the unperturbed chain and, hence, according to our scaling analysis, the criticality should remain. However, it changes the infinite inflation at  $p = p_c$  into a second-order phase transition between a crumpled, random-walk state and a smooth one. In the second part of this chapter we extend the models of pressurized Gaussian and inextensible freely jointed rings in d = 2 to the case where the swelling is caused by a trapped ideal gas of particles. We examine both the canonical and grand-canonical ensembles, in which the particle number Qor the particle fugacity z are fixed, respectively. The chapter is thus divided into two parts. The first (Section 3.2) concerns pressurized rings and the second (Section 3.3) concerns particle-encapsulating rings. Results specific to each scenario are discussed in the corresponding section, while the overall picture of two-dimensional freely jointed rings is summarized in Section 3.4.

# 3.2 Swelling of Pressurized Rings

We start the investigation with the scenario of pressurized rings and define the studied model in Section 3.2.1. Several analytical approaches are used (Sections 3.2.2–3.2.4) as well as Monte Carlo Simulations (Section 3.2.5) in order to study the swelling of such a system. Results concerning this specific system are summarized and discussed in Section 3.2.6.

# 3.2.1 Model

The system under consideration is illustrated in Fig. 3.1. A closed, two-dimensional, freely jointed chain of N monomers is subject to an inflating 2D pressure differential p > 0 between its interior and exterior. The monomers are connected by rigid links of length l. We define  $l \equiv 1$  as the unit of length and the thermal energy  $k_{\rm B}T \equiv 1$ as the unit of energy. (Thus, p is measured in units of  $k_{\rm B}T/l^2$ .) The chain is ideal, *i.e.*, there are no interactions between monomers. (Effects related to self-avoidance will be briefly discussed in Sections 3.2.2 and 3.2.6, and will be studied in detail in Chapter 4.) In addition, no bending rigidity is taken into account, *i.e.*, the chain is freely jointed. A configuration of the ring is defined by a set of 2D vectors  $\{\mathbf{r}_j\}_{j=0...N}$ specifying the positions of the monomers. The condition that the chain be closed is expressed by  $\mathbf{r}_0 = \mathbf{r}_N$ .



Figure 3.1: Schematic illustration of the ring and its parameters.

The probability of a specific configuration is

$$P(\{\mathbf{r}_{j}\}, p) \propto e^{pV[\{\mathbf{r}_{j}\}]} \prod_{j=1}^{N} \delta(|\mathbf{r}_{j} - \mathbf{r}_{j-1}| - 1), \qquad (3.1)$$

where V is the area (two-dimensional volume) enclosed by the ring. As in previous works [75, 85, 86, 90, 91, 92], we take V as the *algebraic* area rather than the geometrical one,

$$V[\{\mathbf{r}_j\}] = \frac{1}{2} \sum_{j=1}^{N} (\mathbf{r}_{j-1} \times \mathbf{r}_j) \cdot \hat{\mathbf{z}}, \qquad (3.2)$$

where  $\hat{\mathbf{z}}$  is a unit vector perpendicular to the 2D plane of the ring. This area may take both positive and negative values. At zero pressure both signs are equally favorable and the mean area must vanish. At high pressures the probability of configurations with negative V is exponentially small in p|V|, and whether one takes the algebraic or geometrical area will become statistically insignificant. (We shall further discuss this assumption in Section 3.2.6.)

Using Eqs. (3.1) and (3.2), we write the partition function of the ring as

$$Z(p,N) = \int \prod_{j=1}^{N} d\mathbf{r}_{j} e^{\frac{1}{2}p(\mathbf{r}_{j-1} \times \mathbf{r}_{j}) \cdot \hat{\mathbf{z}}} \delta(|\mathbf{r}_{j} - \mathbf{r}_{j-1}| - 1).$$
(3.3)

# 3.2.2 Flory Argument

We begin the analysis with a simple Flory argument (see Section 1.1.3) which captures most of the physics to be more rigorously treated in the following sections. The free energy of the ring (in units of  $k_{\rm B}T$ ) is expressed as a function of R, the radius of the statistical cloud of monomers (*i.e.*, the mean radius of gyration). We divide it into three terms,

$$F(R) = F_{\rm el} + F_{\rm inext} + F_p$$
  
$$F_{\rm el} \sim R^2/N, \quad F_{\rm inext} \sim R^4/N^3 \quad F_p \sim -pR^2.$$
(3.4)

The elastic term,  $F_{\rm el}$ , is the usual entropic-spring free energy of a Gaussian chain [1]. The second term is the leading non-Gaussian correction due to the inextensibility of the chain [see Appendix A, Eq. (A.5)], needed here to stabilize the ring against infinite expansion. The last term is the pressure contribution, where the mean volume of the ring is taken as proportional to  $R^2$  [93, 94].

Equation (3.4) has the form of a Landau free energy, describing a second-order transition at  $p = p_c \sim N^{-1}$ . Since the critical pressure depends so strongly on system size, we use hereafter the rescaled pressure  $\hat{p} \equiv p/p_c \sim pN$ , and define the thermodynamic limit as  $N \to \infty$  and  $p \to 0$  such that  $\hat{p}$  is finite. For  $\hat{p} < 1$   $F_{\text{inext}}$  is negligible, and R has a Gaussian distribution with  $\langle R^2 \rangle \sim N(1-\hat{p})^{-1}$ . For  $\hat{p} > 1$  we have  $R^2 \sim N^2(\hat{p}-1)$ . Thus, defining an order parameter M = R/N, we find in the thermodynamic limit

$$M \sim \begin{cases} 0 & \hat{p} < 1\\ (\hat{p} - 1)^{\beta}, \quad \beta = 1/2 & \hat{p} > 1. \end{cases}$$
(3.5)

At the critical point itself  $F = F_{\text{inext}} \sim R^4/N^3$ , and R has a non-Gaussian distribution with

$$\langle R^2(\hat{p}=1) \rangle \sim N^{2\nu_c}, \ \nu_c = 3/4.$$
 (3.6)

Note that the competition between  $F_{\rm el}$  and  $F_p$ , leading to the second-order transition, is unique to 2D. In addition, when an excluded-volume term,  $F_v \sim N^2/R^2$ , is added to the free energy, Eq. (3.4), the transition is removed. This agrees with previous studies of self-avoiding rings [25, 73, 74], which did not report any phase transition upon increasing pressure, and will be further discussed in the following chapter.

# 3.2.3 Mean-Field Theory

In this section we calculate the partition function of the freely jointed ring, Eq. (3.3), by relaxing the rigid delta-function constraints on link lengths into harmonic potentials. The spring constant  $\lambda$  of the links is chosen so as to make the root-mean-square length of a link equal to l = 1. This type of approximation, first suggested by Harris and Hearst [105], was successfully employed in studies of the Karatky-Porod wormlike-chain model [105, 106, 107], where it was shown to be equivalent to a mean-field assumption (for the field conjugate to the rigid link-length constraints) [106, 107]. The partition function contains now only Gaussian terms and, therefore, can be calculated exactly,

$$Z(p, N, \lambda) = \int \prod_{j=1}^{N} d\mathbf{r}_{j} e^{\frac{1}{2}p\mathbf{r}_{j-1} \times \mathbf{r}_{j} - \lambda(\mathbf{r}_{j} - \mathbf{r}_{j-1})^{2}}$$

$$= \frac{1}{\lambda^{N}} \frac{Np}{4\lambda \sin\left(\frac{Np}{4\lambda}\right)}.$$
(3.7)

(The spring constant  $\lambda$  is in units of  $k_{\rm B}T/l^2$ .) Details of the calculation can be found in Ref. [75]. This result can be obtained also by analogy to the quantum propagator of a charged particle in a magnetic field [108]. The mean volume is obtained by differentiation with respect to p,

$$\langle V(p, N, \lambda) \rangle = \frac{\partial \ln Z}{\partial p} = \frac{1}{p} - \frac{N \cot\left(\frac{Np}{4\lambda}\right)}{4\lambda}.$$
 (3.8)

For  $\lambda = 1$  Eq. (3.8) is the same as the result obtained by Rudnick and Gaspari [75, 85, 86], exhibiting a divergence at

$$p_{\rm c} = 4\pi/N. \tag{3.9}$$

Yet, in our case  $\lambda$  is not fixed but is to be determined self-consistently to ensure the softened inextensibility constraint. It is clear that, as the pressure increases, the springs must become stiffer to satisfy this constraint. To impose the constraint, we calculate the mean-square link length and set it to 1,

$$\langle (\mathbf{r}_j - \mathbf{r}_{j-1})^2 \rangle = -\frac{1}{N} \frac{\partial \ln Z}{\partial \lambda} = \frac{1}{\lambda} + \frac{p}{N\lambda} \left( \frac{1}{p} - \frac{N \cot\left(\frac{Np}{4\lambda}\right)}{4\lambda} \right) = 1, \quad (3.10)$$

thus obtaining a transcendental equation for  $\lambda(p, N)$ . We combine Eqs. (3.8) and (3.10) to get a simpler expression for  $\langle V \rangle$  as a function of  $\lambda$ ,

$$\langle V(p, N, \lambda) \rangle = \frac{N(\lambda - 1)}{p}.$$
 (3.11)

Numerical solution of Eq. (3.10) for  $\lambda$  [in the range  $\lambda > Np/(4\pi)$ ] and substitution of the result in Eq. (3.11) yield the mean volume as a function of p and N. (See dashed curves in Fig. 3.2.)



Figure 3.2: The mean volume in units of  $V_{\text{max}} \sim N^2$  as a function of the rescaled pressure (in units of  $p_c \sim N^{-1}$ ) as obtained from the mean-field approximation. The dashed curves are calculated numerically using Eqs. (3.10) and (3.11), whereas the solid curves (calculated only for  $\hat{p} \geq 1$ ) present the approximation given by Eq. (3.15). Calculations were performed for N = 10 (thin curves) and  $N = 10^5$  (thick curves).

For very low pressures,  $p \ll p_c$ , we expand Eq. (3.8) to first order in p to get

$$\langle V(p \ll p_{\rm c}, N) \rangle = \frac{1}{48} N^2 p,$$
 (3.12)

*i.e.*, a linear dependence on p as expected from linear response. (Recall that at p = 0 the mean algebraic area vanishes.)

For higher pressure we obtain a good approximation for  $\lambda(p, N)$  in the limit  $N \gg 1$ by substituting in Eq. (3.10)  $\cot[Np/(4\lambda)] \simeq [Np/(4\lambda) - \pi]^{-1}$ . This gives

$$\lambda(\hat{p}, N \gg 1) \simeq \frac{\hat{p} + 1 + \frac{1}{N} + \sqrt{(\hat{p} - 1)^2 + \frac{2}{N}(\hat{p} + 1) + \frac{1}{N^2}}}{2},$$
(3.13)

where  $\hat{p} \equiv p/p_c = pN/(4\pi)$  is the rescaled pressure. In the thermodynamic limit Eq. (3.13) reduces to the continuous but nonanalytic function,

$$\lambda(\hat{p}, N \to \infty) = \begin{cases} 1 & \hat{p} < 1\\ \hat{p} & \hat{p} > 1. \end{cases}$$
(3.14)

Equation (3.13) should be regarded as an asymptotic expression in the limit  $Np/(4\lambda) \rightarrow \pi$ , which turns out to be valid for any  $p \ll p_c$ . (A Taylor expansion around this point fails because of the nonanalyticity inferred above.) Substituting Eq. (3.13) in Eq. (3.11) yields an approximate expression for  $\langle V \rangle$  as a function of  $\hat{p}$  and N,

$$\langle V(\hat{p} \ll 1, N \gg 1) \rangle \simeq \frac{N^2}{4\pi} \frac{\hat{p} - 1 + \frac{1}{N} + \sqrt{(\hat{p} - 1)^2 + \frac{2}{N}(\hat{p} + 1) + \frac{1}{N^2}}}{2\hat{p}}.$$
 (3.15)

In the thermodynamic limit, the behavior of  $\langle V \rangle$  around and above the critical pressure is obtained from Eq. (3.15) as

1

$$\langle V \rangle = \begin{cases} \frac{N}{4\pi} \frac{1}{\hat{p}(1-\hat{p})} \xrightarrow{\hat{p} \to 1^{-}} \frac{N}{4\pi} \frac{1}{1-\hat{p}} & 1-\hat{p} \gg N^{-1/2} \\ \frac{N^{3/2}}{4\pi} & |1-\hat{p}| \ll N^{-1/2} \\ \frac{N^2}{4\pi} \frac{\hat{p}-1}{\hat{p}} \xrightarrow{\hat{p} \to 1^{+}} \frac{N^2}{4\pi} (\hat{p}-1) & \hat{p}-1 \gg N^{-1/2}, \end{cases}$$
(3.16)

revealing a continuous (second-order) transition. Below the transition we get the same behavior as in the Rudnick-Gaspari model [75, 85],  $\langle V \rangle \sim N(1-\hat{p})^{-1}$ . Yet, due to the inextensibility in our model, the increase of  $\langle V \rangle$  as  $\hat{p} \to 1^-$  breaks at  $|1-\hat{p}| \sim N^{-1/2}$ . In the transition region,  $|1-\hat{p}| \ll N^{-1/2}$ , which shrinks to a point in the thermodynamic limit, we find  $\langle V \rangle \sim N^{2\nu_c}$ ,  $\nu_c = 3/4$ . Above the transition the ring reaches a smooth state with  $\langle V \rangle \sim N^2(\hat{p}-1)/\hat{p}$ . All of these results agree with the findings of the Flory argument presented in Section 3.2.2 once we identify  $\langle V \rangle \sim \langle R^2 \rangle$ . As p is increased to infinity,  $\langle V \rangle$  tends, as it should, to

$$\langle V(\hat{p} \to \infty, N) \rangle = V_{\text{max}} = \frac{N^2}{4\pi},$$
(3.17)

which is the area of a circle of perimeter N.

Figure 3.2 shows the dependence of  $\langle V \rangle$  on  $\hat{p}$  for N = 10 and  $10^5$  calculated both from the numerical solution of Eqs. (3.10) and (3.11), and using the approximate expression (3.15). For large N the critical behavior becomes apparent, with a transition between two distinct states—one in which  $\langle V \rangle \sim N$  and, hence, in units of  $V_{\text{max}} \sim N^2$ , the mean volume vanishes for  $N \to \infty$ , and another with a mean volume proportional to  $V_{\text{max}} \sim N^2$ . As can be seen in Fig. 3.2, the approximate expression (3.15) is practically indistinguishable from the numerical solution for  $\hat{p} \gtrsim 1$ , even for small N.

The compressibility (defined with respect to the reduced pressure  $\hat{p}$ ) is obtained from Eq. (3.16) as

$$\kappa_T = \frac{1}{V} \frac{\partial V}{\partial \hat{p}} \xrightarrow{\hat{p} \to 1^{\pm}} |\hat{p} - 1|^{-\gamma}, \quad \gamma = 1.$$
(3.18)

At the critical point itself the compressibility diverges with N as

$$\kappa_T(\hat{p}=1) = \frac{1}{2}N^{1/2}.$$
(3.19)

To calculate the mean-square radius of gyration,  $\langle R_g^2 \rangle = N^{-1} \sum |\mathbf{r}_j|^2$  (where  $\mathbf{r}_j$  are measured with respect to the center of mass), we add a  $h \sum |\mathbf{r}_j|^2$  term to the Hamiltonian of Eq. (3.7) and differentiate the resulting partition function with respect to h. This yields

$$\langle R_{\rm g}^2(p,N,\lambda)\rangle = \left.\frac{1}{N} \frac{\partial \ln Z(p,N,\lambda,h)}{\partial h}\right|_{h=0} = \frac{4\lambda - Np\cot\left(\frac{Np}{4\lambda}\right)}{Np^2} = \frac{4\lambda}{Np} \langle V\rangle. \tag{3.20}$$

For  $\hat{p} \ll 1$ , combining this result with Eqs. (3.12) and (3.14), we get  $\langle R_{\rm g}^2 \rangle = N/12$ , which is the well known result for the mean-square radius of gyration of a Gaussian ring (*e.g.*, [1]). For large pressures,  $\hat{p} \ge 1$ , we have from Eq. (3.14)  $\lambda \xrightarrow{N \to \infty} \hat{p} = pN/(4\pi)$ , thereby recovering the relation for an average circle,  $\pi \langle R_{\rm g}^2 \rangle = \langle V \rangle$ .

Figure 3.3 shows the dependence of  $\langle R_g^2 \rangle$  on N at fixed pressure. The data were obtained by substituting the numerical solution for  $\lambda$  [Eq. (3.13)] in Eq. (3.20). The

scaling of  $\langle R_g^2 \rangle$  changes at the critical point  $N_c = 4\pi/p$ . Below the critical point,  $N < N_c, \langle R_g^2 \rangle \sim N$ , as in a Gaussian chain. Above it  $\langle R_g^2 \rangle \sim N^2$ , as in a stretched chain. As *p* decreases, the transition becomes sharper. At exactly  $N = N_c, \langle R_g^2 \rangle$  scales as  $N^{3/2}$ . Thus, the analysis of  $\langle R_g^2 \rangle$  yields the same scaling with *N* as obtained for  $\langle V \rangle$ .



Figure 3.3: Mean-square radius of gyration as a function of N at fixed values of  $p = 10^{-5}, 10^{-3}$  and  $10^{-1}$  (thick, dashed and thin curves, respectively) as obtained from the mean-field theory. For  $N < N_c = 4\pi/p$  (marked with arrows)  $\langle R_g^2 \rangle \sim N$ , while for  $N > N_c \langle R_g^2 \rangle \sim N^2$ . At the critical point (diamonds)  $\langle R_g^2 \rangle$  is proportional to  $N^{3/2}$ . The dotted lines show, from bottom to top, the dependencies for an unpressurized ring ( $\langle R_g^2 \rangle = N/12$ ), for a ring at the critical pressure [ $\langle R_g^2 \rangle = N^{3/2}/(4\pi^2)$ ] and for a stretched circle [ $\langle R_g^2 \rangle = N^2/(4\pi^2)$ ].

# 3.2.4 Transfer-Matrix Formulation

Since the interactions between all adjacent monomers are identical, including the one between the first and the Nth, the partition function may be rewritten in the following transfer-matrix form:

$$Z(p,N) = \prod_{\{\mathbf{r}_j\}} \prod_{j=1}^N T(\mathbf{r}_{j-1},\mathbf{r}_j),$$
  
$$T(\mathbf{r},\mathbf{r}') = e^{\frac{p}{2}(\mathbf{r}\times\mathbf{r}')\cdot\hat{\mathbf{z}}}\delta(|\mathbf{r}-\mathbf{r}'|-1).$$
 (3.21)

Solution of the associated eigenvalue problem,

$$\mu \Psi(\mathbf{r}) = \int d\mathbf{r}' T(\mathbf{r}, \mathbf{r}') \Psi(\mathbf{r}'), \qquad (3.22)$$

(in particular, finding the two eigenvalues  $\mu$  of largest absolute value) will yield the exact solution of the model.

Two properties of the operator T are readily noticed: it is non-Hermitian,  $T(\mathbf{r}, \mathbf{r}') \neq T(\mathbf{r}', \mathbf{r})$ , and it is rotational-invariant. To exploit the invariance to rotations, we change to polar coordinates,  $\mathbf{r} = (\rho, \varphi)$ , and separate variables as  $\Psi(\mathbf{r}) = \Omega(\rho)e^{im\varphi}$ , where  $m = 0, \pm 1, \pm 2, \ldots$  to maintain periodicity in  $\varphi$ . Equation (3.22) can then be integrated over angles to give

$$\mu\Omega(\rho) = \int_{\rho-1}^{\rho+1} d\rho' \tilde{T}(\rho, \rho')\Omega(\rho')$$
$$\tilde{T}(\rho, \rho') = \frac{2\cosh\left(p\rho\rho'\sqrt{1-\Delta^2}/2 + im\cos^{-1}\Delta\right)}{\rho\sqrt{1-\Delta^2}}$$
$$\Delta(\rho, \rho') = \frac{\rho^2 + {\rho'}^2 - 1}{2\rho\rho'},$$
(3.23)

thus reducing the original operator to the one-dimensional operator T.

Unfortunately, we have not been able to diagonalize  $\tilde{T}$  for any p. For  $p \gg p_c$ , nevertheless, the ring has stretched configurations, and we can assume that the distances of all monomers from the center of mass are much larger than the link length,  $\rho \gg 1$ . We expand  $\Omega(\rho')$  around  $\rho$  to zeroth order, change variables according to  $\rho' = \rho + \sin \theta$ , and integrate over  $\theta$  to get

$$\mu^{(0)}\Omega(\rho) = 2\pi I_0(p\rho/2)\Omega(\rho), \qquad (3.24)$$

where  $I_0$  is the zeroth-order modified Bessel function of the first kind. Thus, at this order of approximation, the eigenfunctions have the form  $\Omega_k^{(0)}(\rho) = [N/(2\pi\rho_k)]^{1/2}\delta(\rho - \rho_k)$  with a continuous spectrum of eigenvalues. The spectrum is bounded from above by  $\mu_{\max}^{(0)} = 2\pi I_0(p\rho_{\max}/2) = 2\pi I_0[pN/(4\pi)]$ , where  $\rho_{\max} = N/(2\pi)$  is the radius of a perfect circle of perimeter N. (The value of  $\rho_{\max}$  can also be obtained from the condition that  $\int |\Omega(\rho)|^2 d\rho \ge 1$ , *i.e.*, that going from the center of mass outward, one must cross the ring at least once.)

Within the zeroth-order approximation, and in the thermodynamic limit, the par-

tition function is given by

$$Z^{(0)}(p,N) = [\mu_{\max}^{(0)}]^N = [2\pi I_0(pN/4\pi)]^N.$$
(3.25)

This result has a straightforward interpretation. As shown in Appendix A [Eq. (A.1)], it is identical to the partition function of a 2D, open, freely jointed chain subject to a tensile force  $f = pN/(4\pi)$ . This force is just the tension associated with a Laplace pressure p acting on a circle of radius  $\rho_{\text{max}} \sim N$ . The mean volume is obtained from Eq. (3.25) as

$$\langle V(\hat{p}, N) \rangle = \frac{\partial \ln Z}{\partial p} = \frac{N^2}{4\pi} \frac{I_1(\hat{p})}{I_0(\hat{p})},\tag{3.26}$$

which saturates, as expected, to  $V_{\text{max}} = N^2/(4\pi)$  as  $p \to \infty$ . The approach to saturation is given by

$$\langle V(\hat{p} \gg 1) \rangle / V_{\text{max}} \simeq 1 - \frac{1}{2\hat{p}},$$
(3.27)

which corrects the mean-field prediction, Eq. (3.16), by a factor of 2.

# **3.2.5** Monte Carlo Simulations

Since our Flory argument and mean-field theory may fail near the critical point, we conducted Monte Carlo simulations to obtain the mean volume  $\langle V \rangle$ , mean-square radius of gyration  $\langle R_g^2 \rangle$  and mean-square volume fluctuation  $\langle \Delta V^2 \rangle$  as a function of pressure p for different ring sizes N.

## Numerical Scheme



Figure 3.4: Schematic view of a section of the simulated polygon. A randomly chosen vertex (marked by a circle) can be moved to a single position only (marked by a diamond) so as to maintain the lengths of the two links attached to it constant. The area enclosed by the resulting rhomb is the difference in total polygon area for the given step.

We consider a polygon of N equal edges, defined by the 2D coordinates of its vertices. An off-lattice simulation is used, *i.e.*, the positions of the vertices are defined in continuous space. At each step a random vertex is chosen and moved to the only other position that satisfies the edge-length constraint (Fig. 3.4). The difference in energy between the two steps is proportional to the difference in total area, which in turn is simply given by the area of the rhomb composed of the two edges prior to and after the move (see Fig. 3.4). This way each step takes only O(1) operations. The move is subsequently accepted or rejected according to the Metropolis criterion. (See Section 1.1.6.)

The initial configuration is a stretched, regular polygon. This initial condition and the dynamics defined above imply that the polygon angles are restricted to change in discrete quanta of  $\pm 2\pi/N$ . Thus, although the algorithm is off-lattice, the simulated ring is a discrete variant of a freely jointed chain which strictly coincides with the freely jointed model only for  $N \to \infty$ .

The simulations were performed for N between 50 and 3200, and for p between 0 and  $4p_c$ . Away from the critical point, the number of steps required for equilibration is  $O(N^3)$ , but near  $p_c$  the simulation length must be extended due to critical slowing down [109]. This limited our investigation of the transition to  $N \leq 3000$ .

### Results

Figure 3.5 shows simulation results for the mean volume as a function of pressure for different values of N. When p is scaled by  $p_c \sim N^{-1}$  and  $\langle V \rangle$  by N (below  $p_c$ ) or by  $V_{\text{max}} \sim N^2$  (above  $p_c$ ), the data below and above the transition collapse onto two universal curves, thus confirming the predicted scaling laws (see Section 3.2.3) and corresponding to the crumpled and smooth states. However, while the data well below  $p_c$  coincide with the scaling function obtained from the mean-field approximation, Eq. (3.15), the data above the critical pressure collapse onto a different curve.

The simulation results for the mean volume and compressibility at  $p = p_c$  as a function of N are shown in Fig. 3.6A. The reduced compressibility, defined in Eq. (3.18), was calculated from the measured mean-square volume fluctuation as  $\kappa_T =$ 



Figure 3.5: Mean volume as a function of pressure below (A) and above (B) the critical point. The pressure is scaled by  $p_c = 4\pi/N$ , and the volume by N in A and by  $V_{\text{max}} = N^2/(4\pi)$  in B. Symbols show the results of MC simulations for different values of N. The dashed lines show the prediction of the mean-field theory in the limit  $N \to \infty$ .

 $4\pi \langle \Delta V^2 \rangle / (\langle V \rangle N)$ . We get

$$\langle V(p=p_{\rm c})\rangle = (0.102 \pm 0.007)N^{1.49\pm0.01}$$
 (3.28)

$$\kappa_T(p = p_c) = (0.56 \pm 0.09) N^{0.495 \pm 0.025}.$$
 (3.29)

Hence, the mean-field exponents for the scaling with N, Eqs. (3.16) and (3.19), are confirmed. The predicted prefactor of the compressibility is within the standard error of the fit while that of the mean volume is shifted by 4 standard errors.

We also measured from simulations the dependence of the mean-square radius of gyration on N, as depicted in Fig. 3.6B. As predicted, below the critical pressure we find  $\langle R_{\rm g}^2 \rangle \sim N^{1.01\pm0.02}$ , and above it  $\langle R_{\rm g}^2 \rangle \sim N^{1.985\pm0.011}$ . At  $p = p_{\rm c}$  we get

$$\langle R_{\rm g}^2(p=p_{\rm c})\rangle = (0.043 \pm 0.025)N^{1.46\pm0.13}.$$
 (3.30)

For illustration we show in Fig. 3.7 four randomly chosen conformations of an 1600-segment ring at the critical pressure. The shapes vary in size significantly due to critical fluctuations.

The simulation results for the smooth state,  $p > p_c$ , are shown in Fig. 3.8, where they can be compared with the transfer-matrix calculation, Eq. (3.26), and the meanfield results, Eqs. (3.10) and (3.11). On the one hand, there is good agreement with the transfer-matrix calculation for  $\hat{p} \gtrsim 5$ , particularly compared to the mean-field



Figure 3.6: (A) Mean volume and compressibility at  $p = p_c$  as a function of N obtained by MC simulations. The fits  $\langle V(p_c) \rangle = (0.102 \pm 0.007) N^{1.49 \pm 0.01}$  and  $\kappa_T(p_c) = (0.56 \pm 0.09) N^{0.495 \pm 0.025}$  are given by the solid lines. (B) Mean-square radius of gyration as a function of N at different values of  $p = \frac{1}{2}p_c$ ,  $p_c$  and  $2p_c$  with best fits (solid lines)  $\langle R_g^2(\frac{1}{2}p_c) \rangle = (0.12 \pm 0.01) N^{1.01 \pm 0.02}$ ,  $\langle R_g^2(p_c) \rangle = (0.043 \pm 0.025) N^{1.46 \pm 0.13}$ , and  $\langle R_g^2(2p_c) \rangle = (0.019 \pm 0.001) N^{1.985 \pm 0.011}$ .

result. On the other hand, the mean-field theory succeeds in reproducing the phase transition, whereas the zeroth-order transfer-matrix calculation is invalid for these low pressures.

#### **Critical Exponents**

We have confirmed the predicted exponents relating  $\langle V \rangle$ ,  $\langle R_g^2 \rangle$  and  $\kappa_T$  at  $p = p_c$  with the system size N. We now turn to the exponents characterizing the divergence with  $|\hat{p} - 1|$ . As in any continuous phase transition, the critical fluctuations make it hard to accurately measure these critical exponents. Instead, we choose the more reliable route of finite-size scaling to obtain the relations between them. (See Section 1.1.6.)

Let us divide the ring at the critical state into Pincus correlation blobs [19] (see also Section 1.1.5) of g monomers and diameter  $\xi$  each, such that within a blob the polymer behaves as an unperturbed random chain, *i.e.*,  $g \sim \xi^2$ , whereas the chain of blobs is stretched by the pressure. The perimeter of the ring is  $R \sim (N/g)\xi \sim N/\xi$ . We have already established that the perimeter of the ring at  $p = p_c$  scales as  $R \sim N^{3/4}$ . (See Fig. 3.6B.) Thus, for a finite-size system, we get a correlation length which diverges at  $p = p_c$  as

$$\xi(p = p_{\rm c}) \sim N^{1/4}.$$
 (3.31)



Figure 3.7: Four random conformations of a ring with N = 1600 at the critical state as obtained by MC simulations, demonstrating the critical fluctuations. (The positions of the rings have no significance.) The spacing between gridlines is ten times the link length. The dotted circle, shown for reference, has an area (2D volume) equal to the mean area of the ring at this state.

On the other hand, close to the critical point the correlation length diverges as  $\xi \sim |\hat{p}-1|^{-\nu}$ , the compressibility as  $\kappa_T \sim |\hat{p}-1|^{-\gamma}$ , and the order parameter increases as  $M \sim |\hat{p}-1|^{\beta}$ . Using Eq. (3.31) and the numerically established results,  $M = R/N \sim N^{-1/4}$  and  $\kappa_T \sim N^{1/2}$ , we obtain the relations

$$\beta = \nu, \quad \gamma = 2\nu, \tag{3.32}$$

which hold for the mean-field universality class. (Note that the exponents  $\alpha$  and  $\delta$  are irrelevant for this system, since both the ordering field and temperature are incorporated in the single parameter p.)

# 3.2.6 Discussion

We have demonstrated that the swelling of a 2D freely jointed ring due to a pressure differential exhibits a second-order smoothening transition of the mean-field universality class. Below the critical pressure the ring behaves as a random walk, with both the mean volume  $\langle V \rangle$  and mean-square radius of gyration  $\langle R_g^2 \rangle$  proportional to N. In



Figure 3.8: Mean volume (scaled by  $V_{\text{max}}$ ) as a function of pressure (scaled by  $p_c$ ), as obtained by the zeroth-order transfer-matrix calculation (solid curve), mean-field approximation (dashed curve), and MC simulations for N = 1600 (error bars).

this crumpled state the mean volume obeys the scaling  $\langle V \rangle = N f_p^{<}(p/p_c)$ . Mean-field theory accurately captures the scaling law as well as the scaling function  $f_p^{<}$ . (See Fig. 3.5A.) This lies in the fact that, for an unstretched chain, the Gaussian-spring description in the mean-field calculation and the actual freely jointed model coincide as  $N \to \infty$ .

Above the critical pressure  $\langle V \rangle$  and  $\langle R_g^2 \rangle$  are proportional to  $N^2$ . For this smooth state, the scaling conjecture of Chapter 2 holds and a single scaling law exists  $\langle V \rangle = N^2 f_p^>(p/p_c)$  (Fig. 3.5B). This scaling law is also obtained from the mean-field theory, yet this theory fails to predict the correct scaling function  $f_p^>$ . This is because in a stretched state the entropy of a chain of Gaussian, variable springs is much larger than that of a freely jointed chain of rigid links. For  $p \gg p_c$  we have calculated  $f_p^>$  exactly [Eq. (3.26) and Fig. 3.8].

At the transition point itself a new state of polymer chains has been discovered, with  $\langle V \rangle$  and  $\langle R_g^2 \rangle$  proportional to  $N^{2\nu_c}$ ,  $\nu_c = 3/4$ . The swelling exponent  $\nu_c$  turns out to be identical to that of a 2D self-avoiding walk, although the physical origins of the two exponents are unrelated; the freely jointed ring in this intermediate state between crumpled and smooth behaviors contains numerous intersections, as is clearly seen in Fig. 3.7.

One of the strongest assumptions underlying our analysis, as well as those of Refs. [75, 85, 86], is the replacement of the actual geometrical area of the ring with its algebraic area. An important issue is how this assumption affects our results concerning the transition. It is clear that negative contributions to the algebraic area are significant in the crumpled, random-walk state and insignificant in the smooth state. The key question, therefore, is whether they are statistically significant at the transition. Returning to Fig. 3.7 and the blob analysis presented in Section 3.2.5, we infer that the negative area contributions lie only within the correlation blobs. We have shown that each blob contains  $g \sim \xi^2 \sim N^{1/2}$  monomers. The deviation of the geometrical area of a blob from its algebraic area is  $\langle \delta V^2 \rangle^{1/2} \sim \xi^2 \sim N^{1/2}$ . (Recall that the blob contains an unperturbed chain with zero mean algebraic area.) The ring contains  $N/g \sim N^{1/2}$ such blobs. Hence, the total deviation of the geometrical area from the algebraic one is  $(N\langle \delta V^2 \rangle/g)^{1/2} \sim N^{3/4}$ . In the limit  $N \to \infty$  this is negligible compared to the mean area (2D volume) of the ring at the critical state,  $\langle V \rangle \sim N^{3/2}$ . Thus, we conjecture that the same smoothening transition as the one reported here will be found also in a model which considers the geometrical area rather than the algebraic one.

An extension of this model including a non-vanishing bending rigidity was treated by others in a follow-up work [76] and essentially leads to a redefinition of the link length and the number of monomers. (See also Section 1.1.2.) Bending rigidity, thus, is not a relevant parameter and the transition is not removed.

# 3.3 Swelling of Particle-Encapsulating Rings

We now continue to the second studied scenario of this chapter — that of particleencapsulating rings, where both Gaussian and inextensible freely jointed rings are treated. We define the model in Section 3.3.1, and in Section 3.3.2 we derive exact results for a Gaussian ring swollen by trapped particles. We then treat the swelling of a freely jointed ring in Section 3.3.3 by employing a Flory argument, mean-field calculation and Monte Carlo simulations. In addition, we derive exact asymptotes for the large-swelling regime. Finally, the results for particle-encapsulating rings are discussed in Section 3.3.4.

# 3.3.1 Model

We model a 2D polymer ring as a closed ideal chain of N monomers and no bending rigidity. The ring encapsulates an ideal gas of particles. We shall consider separately the two cases of a Gaussian and a freely jointed chain. The monomer-monomer link length is taken as the unit length,  $l \equiv 1$ . For a freely jointed chain this length remains fixed under swelling. For a Gaussian chain, however, the link length has a statistical distribution that varies with swelling; l is then defined as the unperturbed root-meansquare link length.

In a canonical ensemble, where the number Q of particles is fixed, the partition function is given, up to a constant prefactor, by

$$Z(N,Q) = \int_0^\infty dV P_0(N,V) V^Q/Q!,$$
 (3.33)

where V is the 2D volume (*i.e.*, area) bounded by the ring, and  $P_0(N, V)$  is the probability distribution function of the volume for an unpressurized N-monomer ring (for either a Gaussian or a freely jointed chain). From Eq. (3.33) the mean volume of the ring is given by

$$\langle V(N,Q)\rangle = Z^{-1} \int dV V P_0(N,V) V^Q/Q! = (Q+1)Z(N,Q+1)/Z(N,Q).$$
 (3.34)

In a grand-canonical ensemble, where the particles are in contact with a reservoir of fixed fugacity z, we use Eq. (3.33) to write the grand partition function as

$$\mathcal{Z}(N,z) = \sum_{Q=0}^{\infty} Z(N,Q) z^Q = \int_0^{\infty} dV P_0(N,V) e^{zV}.$$
(3.35)

The mean volume in this ensemble is given, therefore, by

$$\langle V(N,z)\rangle = \partial \ln \mathcal{Z}/\partial z,$$
 (3.36)

and the mean particle number by

$$\langle Q(N,z)\rangle = \partial \ln \mathcal{Z}/\partial \ln z = z \langle V \rangle.$$
 (3.37)

Equation (3.36) arises from the fact that the gas of particles is ideal and, hence, their

pressure is equal to their fugacity. According to Eq. (3.37) the mean particle density,  $c = \langle Q \rangle / \langle V \rangle$ , is also equal to the fugacity z, as it should for an ideal gas.

In the grand-canonical ensemble fluctuations in particle number and in ring volume are correlated. The correlation is characterized by the following covariance,

$$C_{QV}(N,z) = \frac{\langle QV \rangle - \langle Q \rangle \langle V \rangle}{\langle Q \rangle \langle V \rangle}.$$
(3.38)

From Eq. (3.35) we find

$$\langle QV \rangle = \frac{1}{\mathcal{Z}} \frac{\partial^2 \mathcal{Z}}{\partial (\ln z) \partial z} = z \langle V^2 \rangle,$$
 (3.39)

which, combined with Eq. (3.37), yields

$$C_{QV}(N,z) = \frac{\langle \Delta V^2 \rangle}{\langle V \rangle^2}, \qquad (3.40)$$

where  $\langle \Delta V^2 \rangle = \langle V^2 \rangle - \langle V \rangle^2$  is the mean-square volume fluctuation. Hence, interestingly, in the grand-canonical ensemble the cross-correlation of Q and V is identical to the relative mean-square fluctuation in the ring volume.

Several complications related to the definition of the ring volume in the model should be mentioned. In principle the V appearing in Eq. (3.33) should be the geometrical area  $V_{\rm g}$  of the ring, since it is  $V_{\rm g}$  that determines the translational entropy of the particles. As in Section 3.2 and previous works [75, 85, 86], however, we are technically bound to use the *algebraic* area V instead. This area (2D volume) may contain both positive and negative contributions,  $V_+$  and  $V_-$ . In an unperturbed ring positive and negative areas are equally favorable, and the mean algebraic area then vanishes. (The algebraic area may also "count" a certain geometrical-area contribution more than once due to chain winding.) On the one hand, particle entropy forces us to use only the positive-area part of  $P_0$  (hence the integration from 0 to  $\infty$  in Eq. (3.33)). Consequently, the mean algebraic area of an unperturbed ring,  $\langle V \rangle$ , does not vanish. This is the definition used in the analytical parts of this work. In the simulations, on the other hand, we follow changes in the actual algebraic area of the ring, allowing the total area to become negative. Thus, in the numerical parts of this work  $\langle V \rangle$  of an unperturbed ring does vanish. In addition, the simulated particles are placed only inside positive parts of the ring area, *i.e.*, their entropy-relevant area is  $V_+ \neq V$ . Finally, in Eq. (3.35) one notices a direct analogy between the problem of fixed particle fugacity studied here and that of an empty ring subject to a fixed pressure, as studied in Section 3.2 and in Ref. [85]. The mapping is not exact, however, since in the current case V is restricted to positive values, whereas in the previous section and [85] it was not. All these subtleties are significant only in the weak-swelling regime of small volumes. As the inner pressure exerted by the particles increases, the distinction between the various volume definitions becomes negligible and does not affect our main results, as will be demonstrated below.

# 3.3.2 Gaussian Ring

In this section we consider a 2D Gaussian ring swollen by trapped particles, for which exact results can be derived. The chain consists of a set of N springs with fixed spring constant,  $\lambda = 1$ , in units of  $k_{\rm B}T/l^2$  (to yield an unperturbed root-mean-square spring length of l = 1). For the sake of the following sections, in which the spring constant is allowed to change, we keep the results dependent on  $\lambda$  without substituting  $\lambda = 1$ .

## **Canonical Ensemble**

The probability distribution function of the algebraic area for a 2D Gaussian ring was calculated by Khandekar and Wiegel [90, 91, 92],<sup>2</sup>

$$P_0^{\rm G}(N,V) = \frac{1}{\lambda^N} \frac{2\pi\lambda}{N\cosh^2(2\pi\lambda V/N)}.$$
(3.41)

Substituting Eq. (3.41) in Eq. (3.33), we obtain the exact partition function,

$$Z^{\mathcal{G}}(N,Q) = \frac{2}{\lambda^{N}} \left(\frac{N}{4\pi\lambda}\right)^{Q} (1-2^{1-Q})\zeta(Q), \qquad (3.42)$$

where  $\zeta$  is the Riemann zeta function. The mean volume is then given, according to Eq. (3.34), by

$$\langle V^{\rm G}(N,Q)\rangle = \frac{N(Q+1)}{4\pi\lambda} \frac{1-2^{-Q}}{1-2^{1-Q}} \frac{\zeta(Q+1)}{\zeta(Q)},$$
 (3.43)

<sup>&</sup>lt;sup>2</sup>Equation (3.41) differs from the original Khandekar-Wiegel expression by a factor of 2, since the particle translational entropy in the current model restricts our analysis to positive volumes (Eq. (3.33)).

which turns, in the limit of large Q, to

$$\langle V^{\rm G}(N,Q\gg 1)\rangle = [N^2/(4\pi\lambda)](Q/N).$$
 (3.44)

In the current case of fixed  $\lambda$ , we thus get that the ring swells gradually (linearly) with Q. This is qualitatively different from the Rudnick-Gaspari result for the swelling as a function of fixed pressure [75, 85, 86], where the mean volume diverges at a finite critical pressure,  $p_{\rm c} = 4\pi/N$  (in units of  $k_{\rm B}T/l^2$ ). The ability of the Gaussian ring to swell indefinitely stems, as in the Rudnick-Gaspari model, from its extensibility.

Since the mean volume is proportional to Q, we obtain in this ensemble the peculiar result that the particle density is independent of particle number,

$$c^{\rm G}(N) = Q/\langle V^{\rm G} \rangle = 4\pi\lambda/N. \tag{3.45}$$

The same holds for the particle fugacity,

$$z^{\rm G}(N) = \exp(-\partial \ln Z^{\rm G}/\partial Q) = 4\pi\lambda/N, \qquad (3.46)$$

which is equal to the density of Eq. (3.45), as expected for an ideal gas. The mean pressure of the gas, in our dimensionless units, is  $p = c = 4\pi/N$ . (Recall that  $\lambda = 1$ .) Thus, for any Q the ring swells to such an extent that the pressure exerted on it by the gas is always at the Rudnick-Gaspari  $p_c$ , yet without the associated criticality.

#### **Grand-Canonical Ensemble**

The grand partition function is obtained from Eqs. (3.35) and (3.41) as

$$\mathcal{Z}^{\rm G}(N,z) = \frac{1}{\lambda^{N+1}} \left[ -\lambda + \psi(-x) - \psi(1/2 - x) \right], \tag{3.47}$$

where  $x \equiv zN/(8\pi\lambda)$ , and  $\psi$  is the digamma function (the logarithmic derivative of the gamma function). The mean volume is calculated according to Eq. (3.36), yielding

$$\langle V^{\rm G}(N,z)\rangle = \frac{1}{\lambda^N \mathcal{Z}^{\rm G}} \frac{N}{4\pi\lambda} \left\{ \psi(-x) - \psi(1/2 - x) - x \left[ \psi'(-x) - \psi'(1/2 - x) \right] \right\}, \quad (3.48)$$

where a prime denotes a first derivative. The mean number of trapped particles, according to Eq. (3.37), is simply given by  $\langle Q^{\rm G} \rangle = z \langle V^{\rm G} \rangle$ .

The digamma function and its derivative diverge for small arguments as  $\psi(x) \simeq$ 

 $-x^{-1}$  and  $\psi'(x) \simeq x^{-2}$ , respectively. Thus, the expressions for  $\mathcal{Z}^{\mathrm{G}}$ ,  $\langle V^{\mathrm{G}} \rangle$ , and  $\langle Q^{\mathrm{G}} \rangle$  diverge at a critical fugacity (with  $\lambda = 1$ ),

$$z_{\rm c} = 4\pi/N.$$
 (3.49)

Since for the ideal gas p = c = z, this divergence is analogous to that of the Rudnick-Gaspari model at  $p_c = 4\pi/N$ .

# 3.3.3 Freely Jointed Ring

We now turn to the case of a freely jointed chain, *i.e.*, an inextensible ring whose link lengths are fixed.

#### **Canonical Ensemble**

#### Flory Argument

We begin by examining a simple Flory argument, as demonstrated above (Section 3.2.2). The free energy of the ring (in units of  $k_{\rm B}T$ ) is expressed as a function of R, the radius of the statistical cloud of monomers (*i.e.*, the radius of gyration). As in Section 3.2.2 we divide it into three terms,

$$F(R,Q) = F_{\rm el} + F_{\rm inext} + F_{\rm en},$$
(3.50)  
$$F_{\rm el} \sim R^2/N, \quad F_{\rm inext} \sim R^4/N^3, \quad F_{\rm en} \sim Q[\ln(Q/R^2) - 1].$$

The first two terms are identical to those used under fixed pressure in Eq. (3.4), the first being the usual entropic-spring free energy of a Gaussian chain [1], and the second — the leading non-Gaussian correction due to inextensibility (see Appendix A). The last term comes from the translational entropy of the ideal gas, where the mean 2D volume of the ring is taken (as in Section 3.2.2) to be proportional to  $R^2$  [93, 94].

Unlike the case of fixed pressure of Section 3.2, the free energy of Eq. (3.50) exhibits no phase transition with increasing Q. Upon minimization with respect to R we get the following scaling law:

$$R^2 \sim N^2 f_Q(Q/N),$$
 (3.51)

which, despite the crudeness of the Flory argument, is equivalent to the one predicted from the general scaling theory [Chapter 2, Eq. (2.6b)], and will be confirmed below.

### Mean-Field Approximation

We proceed to study the freely jointed model by relaxing the strict constraints of fixed link lengths into harmonic potentials, as performed in Section 3.2.3. The calculation is identical to that for a Gaussian chain (Section 3.3.2), except that the spring constant  $\lambda$  is not fixed but determined self-consistently to maintain the rootmean-square link length equal to l = 1.

To impose the relaxed inextensibility constraint we differentiate  $Z^{G}$  of Eq. (3.42) with respect to  $\lambda$  to get the mean-square link length, and then set it to 1,

$$-N^{-1}\partial \ln Z^{\rm G}/\partial \lambda = (1+\hat{Q})/\lambda = 1, \qquad (3.52)$$

where  $\hat{Q} \equiv Q/N$  is the rescaled particle number. For  $\hat{Q} \to 0$  we get  $\lambda = 1$ , as expected, but as the number of trapped particles increases, the springs get stiffer according to

$$\lambda = 1 + \hat{Q}.\tag{3.53}$$

This value is substituted in Eq. (3.44) to obtain

$$\langle V^{\rm FJ}(N,\hat{Q})\rangle = V_{\rm max}\hat{Q}/(\hat{Q}+1). \tag{3.54}$$

As  $\hat{Q} \to \infty$  the mean area appropriately tends to its maximum value,  $V_{\text{max}} = N^2/(4\pi)$ , which is the area of a circle with perimeter N. Equation (3.54) shows that the swelling of the ring with increasing Q is gradual, without any phase transition.

The particle density is given by

$$c^{\rm FJ}(N,\hat{Q}) = Q/\langle V^{\rm FJ} \rangle = 4\pi (\hat{Q}+1)/N.$$
 (3.55)

The fugacity is found from Eqs. (3.46) and (3.53) as

$$z^{\rm FJ}(N,\hat{Q}) = 4\pi(\hat{Q}+1)/N,$$
 (3.56)

which is equal to  $c^{\text{FJ}}$ , as it should for an ideal gas. The pressure is  $p = z = (4\pi/N)(\hat{Q} + 1)$ , which is larger than  $p_c = 4\pi/N$  for any Q.

### Exact Asymptote for Strong Swelling

In the limit of large particle number,  $\hat{Q} \gg 1$ , the partition function can be calcu-

lated exactly. In this limit the chain is highly swollen and its statistics is governed by large-volume conformations. Thus, to apply Eq. (3.33), we merely need to know how the volume probability distribution function for a 2D freely jointed ring,  $P_0^{\rm FJ}(N, V)$ , decays to zero as V approaches  $V_{\rm max}$ . This calculation is presented in Appendix B. The result is

$$P_0^{\rm FJ}(N, V \lesssim V_{\rm max}) \sim (V_{\rm max} - V)^{N/2}.$$
 (3.57)

Substituting Eq. (3.57) in Eq. (3.33), we get

$$Z^{\rm FJ}(N,Q \gg N) = (V_{\rm max})^{Q+N/2} \frac{\Gamma(1+N/2)}{\Gamma(1+N/2+Q)},$$
(3.58)

where  $\Gamma$  is the gamma function. The mean volume is then obtained from Eq. (3.34) as

$$\langle V^{\rm FJ}(N,\hat{Q}\gg1)\rangle \simeq V_{\rm max}\frac{\hat{Q}}{\hat{Q}+1/2}\simeq V_{\rm max}\left(1-\frac{1}{2\hat{Q}}\right).$$
 (3.59)

Thus, the exact approach of the mean volume to its maximum value differs from the mean-field result, Eq. (3.54), by a factor of 1/2.

#### Monte Carlo Simulations

We performed Monte Carlo simulations to obtain the mean volume  $\langle V \rangle$  of a freely jointed ring as a function of the number Q of trapped ideal-gas particles for various ring sizes N. The algorithm combines an off-lattice scheme for the polymer, as was used in Section 3.2.5, with a lattice model for the particles. The simulated system is schematically shown in Fig. 3.9. The ring is represented by a polygon of N equal edges of length l = 1. The 2D coordinates of the vertices take continuous values. The coordinates of the particles are defined on a 2D square lattice with lattice constant of either l or l/5, depending on the required precision.

The initial configuration is a fully stretched, regular polygon of purely positive algebraic area,  $V = V_+$ . During the simulation we keep track of positive and negative contributions to V and place particles only on lattice sites belonging to  $V_+$ . Each step of the simulation is composed of two actions. In the first, each particle is moved to a randomly chosen juxtaposed lattice site, unless this site is outside the positive-area part of the polygon. In the second action, a randomly chosen chain vertex is moved to the only other position that satisfies the edge-length constraint (see Fig. 3.9). This



Figure 3.9: Schematic view of a section of the simulated system. Point particles (marked by +) are located on lattice sites confined inside the ring. On each step each particle is moved to a randomly chosen neighboring site. In the second part of the step a single randomly chosen chain vertex (marked by a circle) is moved to the only other position (marked by a diamond) that maintains the lengths of the two links attached to it.

action is automatically rejected if it makes a particle leave the positive-area part of the ring. These dynamics involve O(Q) operations per step. The number of operations required for equilibration is  $O(N^3Q)$ , limiting our investigation to  $N \leq 500$ . The simulations were performed for N between 50 and 400 and Q between 0 and 4N.

Figure 3.10 shows the simulation results for the mean volume (scaled by  $V_{\text{max}} \sim N^2$ ) as a function of the rescaled particle number  $\hat{Q} = Q/N$ . All data for different values of N collapse onto a single universal curve, in accord with the scaling law obtained from the Flory argument and mean-field calculation (Eqs. (3.51) and (3.54)). Yet, only for small  $\hat{Q}$  does this curve coincide with the mean-field scaling function. For such small  $\hat{Q}$  it coincides also with the Gaussian result, (Eq. (3.44) with  $\lambda = 1$ ).

To confirm the highly swollen behavior derived in the preceding section we simulated rings of N = 50 with Q between 0 and 50N. The results are presented in Fig. 3.11, showing good agreement for large  $\hat{Q}$  with the exact asymptote, Eq. (3.59).

#### **Grand-Canonical Ensemble**

#### Flory Argument

To account for contact of the particles with a reservoir of fixed fugacity z we add a  $-Q \ln z$  term to the Flory free energy, Eq. (3.50). Minimization with respect to Q



Figure 3.10: Mean volume of a freely jointed ring, scaled by  $V_{\text{max}} \sim N^2$ , as a function of the rescaled number of particles. Monte Carlo simulation results for various values of N are represented by symbols with error bars. The dashed line shows the mean-field result (Eq. (3.54)). The result for a Gaussian ring (Eq. (3.44)) is given for reference (dotted line). The inset focuses on the small  $\hat{Q}$  region using a logarithmic scale.

yields the following grand potential:

$$\mathcal{F}(R, z) = F_{\rm el} + F_{\rm inext} + F_{\rm res}, \qquad (3.60)$$
$$F_{\rm el} \sim R^2/N, \quad F_{\rm inext} \sim R^4/N^3, \quad F_{\rm res} \sim -zR^2.$$

This Landau-like free energy has a second-order phase transition at  $z_{\rm c} \sim N^{-1}$ , similar to the one obtained for fixed pressure in Eq. (3.4). For  $z < z_{\rm c} F_{\rm inext}$  is negligible, and R has a Gaussian distribution with  $\langle R^2 \rangle \sim N(1 - z/z_{\rm c})^{-1}$ . For  $z > z_{\rm c}$  we have  $R^2 \sim N^2(z/z_{\rm c} - 1)$ .

#### Mean-Field Approximation

We apply a relaxed inextensibility constraint (similar to the one applied in the canonical case) by determining the spring constant  $\lambda$  so that the root-mean-square link length should be l = 1. In the current grand-canonical case this is done by



Figure 3.11: Mean volume of a freely jointed ring, scaled by  $V_{\text{max}}$ , as a function of the rescaled particle number, as obtained by Monte Carlo simulations for N = 50 (symbols with error bars). The solid line shows the exact asymptote for a highly swollen ring (Eq. (3.59)). The dashed line presents the mean-field result (Eq. (3.54)).

differentiating  $\mathcal{Z}^{G}$  of Eq. (3.47) with respect to  $\lambda$ ,

$$-N^{-1}\partial \ln \mathcal{Z}^{G}/\partial \lambda = \frac{1}{\lambda} + \frac{2}{\lambda^{N+1}N\mathcal{Z}^{G}}x \left\{\psi(-x) - \psi(1/2 - x) - x \left[\psi'(-x) - \psi'(1/2 - x)\right]\right\} = 1,$$
(3.61)

thus obtaining a transcendental equation for  $\lambda(z, N)$ . Equation (3.61) can be combined with Eq. (3.48) to get a simpler expression for  $\langle V \rangle$  as a function of  $\lambda$ ,

$$\langle V^{\rm FJ}(N,z,\lambda)\rangle = N(\lambda-1)/z.$$
 (3.62)

Numerical solution of Eq. (3.61) for  $\lambda$  and substitution of the result in Eq. (3.62) yield the mean volume as a function of z and N.

We can get a good approximation for  $\lambda(z, N)$  by substituting for the diverging terms in Eq. (3.61)  $\psi(x) \simeq -x^{-1}$  and  $\psi'(x) \simeq x^{-2}$ . This gives

$$\lambda(\hat{z}, N \gg 1) \simeq \frac{\hat{z} + 1 + \frac{1}{N} + \sqrt{(\hat{z} - 1)^2 + \frac{2}{N}(\hat{z} + 1) + \frac{1}{N^2}}}{2},$$
(3.63)

where  $\hat{z} \equiv zN/(4\pi)$  is the rescaled fugacity. This result for  $\lambda$  is the same as the one

obtained for fixed pressure p with p = z. In the thermodynamic limit, defined here as  $N \to \infty$  and  $z \to 0$  such that  $\hat{z}$  is finite, Eq. (3.63) reduces to the continuous but nonanalytic function,

$$\lambda(\hat{z}, N \to \infty) = \begin{cases} 1 & \hat{z} < 1\\ \hat{z} & \hat{z} > 1. \end{cases}$$
(3.64)

Substituting Eq. (3.63) in Eq. (3.62) yields an approximate expression for  $\langle V \rangle$  as a function of  $\hat{z}$  and N,

$$\langle V^{\rm FJ}(\hat{z} \not\ll 1, N \gg 1) \rangle \simeq \frac{N^2}{4\pi} \frac{\hat{z} - 1 + \frac{1}{N} + \sqrt{(\hat{z} - 1)^2 + \frac{2}{N}(\hat{z} + 1) + \frac{1}{N^2}}}{2\hat{z}},$$
 (3.65)

which in the thermodynamic limit becomes

$$\langle V^{\rm FJ} \rangle = \begin{cases} \frac{N}{4\pi} \frac{1}{\hat{z}(1-\hat{z})} \xrightarrow{\hat{z} \to 1^{-}} \frac{N}{4\pi} \frac{1}{1-\hat{z}} & 1-\hat{z} \gg N^{-1/2} \\ \frac{N^{3/2}}{4\pi} & |\hat{z}-1| \ll N^{-1/2} \\ \frac{N^2}{4\pi} \frac{\hat{z}-1}{\hat{z}} \xrightarrow{\hat{z} \to 1^{+}} \frac{N^2}{4\pi} (\hat{z}-1) & \hat{z}-1 \gg N^{-1/2}, \end{cases}$$
(3.66)

thus exhibiting a continuous phase transition at  $\hat{z}_c = 1$ , analogous to the one found for fixed pressure, Eq. (3.16). As shown in Eq. (3.37), the mean number of trapped particles is given by  $\langle Q^{\rm FJ} \rangle = z \langle V^{\rm FJ} \rangle$  and, therefore, undergoes the same transition at  $\hat{z}_c$ .

#### Exact Asymptote for Strong Swelling

As demonstrated above, and also confirmed by simulations in the next section, fixing the fugacity in the grand-canonical ensemble is analogous to fixing the pressure in an empty ring. Thus, to get the asymptotic swelling at high fugacity we can readily use the exact asymptote for high pressure, Eq. (3.26) and replace  $p \rightarrow z$ . This yields

$$\langle V(\hat{z} \gg 1, N) \rangle \simeq V_{\max} \frac{I_1(\hat{z})}{I_0(\hat{z})} \simeq V_{\max} \left(1 - \frac{1}{2\hat{z}}\right),$$
(3.67)

where  $I_n$  are modified Bessel functions of the first kind.

#### Monte Carlo Simulations

We performed grand-canonical Monte Carlo simulations to check the results of the preceding sections. To each step of the algorithm described above (for the canonical

case) a third action is added as follows. Either a randomly chosen particle is removed with probability  $Q/(zV_+)$ , or a particle is added at a randomly chosen site within the positive-area part of the ring with probability  $zV_+/(Q+1)$ .

Fig. 3.12 shows simulation results for different values of N in the crumpled and smooth states,  $\hat{z} < 1$  and  $\hat{z} > 1$ , respectively. The data collapse onto a single universal curve in each state. In the weak-swelling state (Fig. 3.12A) the mean volume scales as  $\langle V \rangle = N f_z^{<}(\hat{z})$ , whereas in the strong-swelling state (Fig. 3.12B) it scales as  $\langle V \rangle = N^2 f_z^>(\hat{z})$ . These results confirm the scaling laws predicted by the Flory argument and mean-field theory, albeit with different scaling functions. The discrepancy in Fig. 3.12A between the simulation results and the mean-field expression stems from the different definitions of the ring volume discussed in Section 3.3.1. In the simulation we measure the actual algebraic area, which vanishes at z = 0. The calculation, however, considers only positive algebraic areas (cf. Eq. (3.33)) and, hence, yields a finite mean volume at zero fugacity,  $\langle V(0) \rangle = N(\ln 2)/(2\pi)$ . When this value of  $\langle V(0) \rangle$  is subtracted from the mean-field result (dotted line in Fig. 3.12A), the agreement with the simulations is excellent, indicating that the mean-field theory does accurately capture the swelling for  $z < z_c$ . On the other hand, the disagreement between simulation and theory in Fig. 3.12B arises from the inadequacy of the mean-field approximation for stretched freely jointed chains, as was observed also in the fixed-p ensemble in Section 3.2. In Fig. 3.12B we compare the data from Section 3.2.5 for a freely jointed chain subject to a pressure  $p > p_c$  with those for fixed fugacity  $z > z_c$ . The two data sets are practically indistinguishable once one identifies p with z.

Due to computation limitations we have not directly confirmed the asymptotic strong-swelling behavior at large  $\hat{z}$  as given by Eq. (3.67); nevertheless, the equivalent asymptote for high pressure was confirmed above (see Fig. 3.8).

To test Eq. (3.40) for the cross-correlation of particle number and ring volume we measured from the simulations the covariance  $C_{QV} = (\langle QV \rangle - \langle Q \rangle \langle V \rangle)/(\langle Q \rangle \langle V \rangle)$ for N = 50 and varying z. The results are presented in Fig. 3.13 alongside the relative mean-square volume fluctuations. The two data sets are indistinguishable, in agreement with Eq. (3.40). (In these measurements the volume was taken as  $V_{+}$ .) As expected, the correlation is appreciable in the crumpled, unpressurized state (small z) and decays to zero as the ring swells into a smooth circle (large z).



Figure 3.12: Mean volume of a freely jointed ring as a function of particle fugacity below (A) and above (B) the critical point. The fugacity is scaled by  $z_c = 4\pi/N$ , and the volume by N in A and by  $V_{\text{max}} = N^2/(4\pi)$  in B. Symbols with error bars show the results of grand-canonical Monte Carlo simulations for different values of ring sizes N. The dashed lines show the mean-field prediction in the limit  $N \to \infty$ . The dotted line in A presents the mean-field result shifted down by  $\langle V(0) \rangle/N = (\ln 2)/(2\pi)$ . Panel B shows also simulation results from Section 3.2.5 for the swelling of a freely jointed ring with pressure p, for which the horizontal axis represents  $\hat{p} = p/p_c$ .

## 3.3.4 Discussion

As suggested by the scaling analysis of Chapter 2, when the number Q of trapped particles is prescribed, we find that the critical behavior, observed for pressurized rings, disappears. The mechanism is qualitatively different from ordinary ones, where criticality is removed by disorder or fluctuations. It lies here in the absence of a volume constraint, *i.e.*, in the freedom of these systems to select their mean volume so as to maximize the total entropy. For a Gaussian ring we have found that the mean volume is  $\langle V \rangle = NQ/(4\pi)$ , implying that the particles exert an effective pressure just equal to  $p_c = 4\pi/N$  for any Q > 0. The volume never diverges, as it does for fixed p, but grows gradually, indefinitely, with increasing Q. For a freely jointed ring, by contrast, the mean volume is such that the exerted pressure remains above  $p_c$  for any Q > 0. As a result, the swollen ring always obeys the smooth-state scaling law,  $\langle V \rangle \sim N^2 f_Q(Q/N)$ . We will return to this point in Chapter 7.

When the particle fugacity z is prescribed, the criticality of the Gaussian and freely-jointed rings is retained. In this case the system does not have the freedom



Figure 3.13: Correlation between particle number and ring volume as a function of particle fugacity, compared to the relative mean-square volume fluctuations. Simulations were performed for an N = 50 ring, and the ring volume was taken as  $V_+$ .

to select the pressure exerted on its boundary, since p is determined by z through the equation of state of the gas (p = z for an ideal gas). The models then become analogous to the fixed-pressure ones, as studied in Section 3.2 and in Ref. [85]. Thus, the canonical and grand-canonical ensembles are inequivalent in these systems. A vivid example is seen in the Gaussian model, where the canonical mean fugacity z is found to be independent of Q [Eq. (3.46)], whereas the grand-canonical mean particle number does vary with z [Eqs. (3.37) and (3.48)] and even diverges at  $z_c$ . The former result of a fugacity independent of particle number is clearly a consequence of the unconstrained volume. We infer, therefore, that this unusual property also underlies the ensemble inequivalence.

In the grand-canonical case we have derived, and confirmed in simulations, an identity relating the correlation between particle number and ring volume with the volume fluctuations [Eq. (3.40) and Fig. 3.13]. The only assumption entering this derivation is the consideration of the particles as an ideal gas. Thus, the same identity should hold for any fluctuating envelope with unconstrained volume, enclosing an ideal gas of particles.

# 3.4 Summary

In this chapter we have seen a first example where the two swelling scenarios — pressurized and particle-encapsulating manifolds — are inequivalent. This inequivalence stems already from the scaling analysis of Chapter 2, which predicts for this model system, *i.e.*, for d = 2 and  $\nu = 1/2$ , criticality in the fixed-*p* scenario and gradual swelling with number of trapped particles.

Both Gaussian rings and freely-jointed ones exhibit criticality with fixed-p. While the former explodes at  $p_c$  due to the extensibility of the links [75, 85], the latter undergoes a continuous transition from crumpled random-walk statistics to a smooth state. For any  $p > p_c$  the swelling obeys a single scaling law,  $\langle V \rangle = N^2 f_p^>(pN)$ , as predicted by Eq. (2.6a) for d = 2 (cf. Fig. 3.5B).

The swelling with Q is gradual in both Gaussian and freely-jointed rings and follows the scaling conjecture, Eq. (2.6b) with d = 2, *i.e.*,  $\langle V \rangle \sim N^2 f_Q(Q/N)$ . For Gaussian rings this is verified analytically [see Eq. (3.44)]. For freely jointed rings, mean-field approximation produces the correct scaling law, Eq. (3.54), yet fails to predict an accurate scaling function  $f_Q$  (see Fig. 3.10).

This study has been restricted to self-intersecting rings. When a self-avoidance term is added to the Flory grand potential, Eq. (3.60), the second-order transition disappears, as in the case of fixed pressure (see Section 3.2.2). This stems out from the form of Eq. (3.60), in which the two terms  $F_{\rm el} \sim R^2$  and  $F_{\rm res} \sim R^2$  may cancel each other regardless of the value of R. Thus, any slight change in the form of the free-energy (which is not  $\sim R^2$ ) will remove this pathological behavior. We note, however, that the Flory argument does not reproduce the correct scaling regimes for pressurized self-avoiding rings as derived in Refs. [25, 73, 74]. We now proceed to test this model system in more detail.

# Chapter 4 Swelling of 2D Self-Avoiding Rings

In this chapter we continue to another two-dimensional example—that of self-avoiding rings. According to the scaling analyses of Chapter 2 both pressurized and particle-encapsulating vesicles should swell gradually without criticality. We test this prediction using Monte Carlo simulations of closed self-avoiding chains subject to either a fixed pressure difference or a fixed number of trapped particles. In accordance with the scaling predictions these two model systems swell gradually, following a single scaling law in each case, and are shown to be thermodynamically equivalent.<sup>1</sup>

# 4.1 Introduction

In the previous chapter we have demonstrated that a two-dimensional freely-jointed ring subject to a pressure difference undergoes a second-order phase transition. It was also noted, based on a Flory argument, that when self-avoidance is introduced, this criticality is removed. Studies of self-avoiding two-dimensional rings subject to a pressure difference p were conducted by Fisher *et al.*, who studied two-dimensional self-avoiding closed chains using tether-and-bead Monte Carlo simulations and scaling analysis [25, 73, 74, 110, 111]. When no perturbation is considered, the rings obey self-avoiding-walk statistics with a mean area (two-dimensional volume)  $\langle V \rangle \sim$  $N^{2\nu}$ ,  $\nu = 3/4$ . For a deflating pressure p < 0 the ring is in a deflated crumpled configuration whose statistics resembles that of branched polymers. For an inflating pressure difference, p > 0, three regimes were found:

<sup>&</sup>lt;sup>1</sup>The results presented in this chapter were published in Ref. [70].

- (i) a weak-inflation crumpled regime for  $0 < pN^{2\nu} \lesssim 1$ , where the mean volume scales as  $\langle V \rangle \sim N^{2\nu} f_p(pN^{2\nu})$ ;
- (ii) a strong-inflation crumpled regime for  $1 \leq pN^{2\nu} \ll N^{2\nu-1}$ , where the same scaling holds but the scaling function  $f_p$  becomes linear,  $\langle V \rangle \sim N^{2\nu}(pN^{2\nu})$ ; and
- (iii) a smooth regime for  $pN^{2\nu} \gtrsim N^{2\nu-1}$ , where  $\langle V \rangle \sim N^2$ .

The crossovers between these regimes are gradual with no phase transitions. More rigorous works on 2D lattice rings confirm most of these findings [112, 113]. In the thermodynamic limit, defined as  $N \to \infty$  and  $p \to 0$  such that  $pN^{2\nu}$  is finite, the range of the scaling regime (ii) in the case of self-avoiding walks ( $\nu = 3/4$ ) occupies the entire relevant swelling regime,  $pN^{2\nu} \in (1, \infty)$ . Note, however, that in the random-walk case ( $\nu = 1/2$ ) regime (ii) shrinks to a point  $pN^{2\nu} \sim 1$ . We demonstrated in Chapter 3 that for random walks regime (ii) turns, in fact, into a second-order phase transition between regimes (i) and (iii). Thus, we infer that self-avoidance acts as a relevant parameter for the critical point discussed in Section 3.2.

According to the scaling analysis presented in Chapter 2, for a two-dimensional self-avoiding ring we have the scaling law conjecture [Eq. (2.6a)],

$$\langle V \rangle \sim N^2 f_p(pN).$$
 (4.1a)

This is *not* in contradiction with the results presented above, since we consider a different thermodynamic limit,  $N \to \infty$  and  $p \to 0$  such that pN is finite. Hence, in this description the first regime (i) shrinks into the point p = 0. The second regime (ii) coincides with the power law dependence given by Eq. (2.5a) for d = 2 and  $\nu = 3/4$ ,  $\langle V \rangle \sim N^2(pN)$ . We will show below that the third regime (iii) also scales according to Eq. (4.1a), and so this scaling relation holds throughout the swelling.

For a particle-encapsulating self-avoiding ring, which is considered for the first time in this work, the scaling conjecture, Eq. (2.6b), predicts gradual swelling,

$$\langle V \rangle \sim N^2 f_Q(Q/N),$$
 (4.1b)

with a power-law dependence,  $\langle V \rangle \sim N^{3/2}Q^{1/2}$ , for small Q. Since no criticality exists in both ensembles, there is supposedly a smooth transform relating the two. This is
shown below to be correct.

In this chapter we perform Monte Carlo simulations of self-avoiding rings in d = 2 to verify the scaling laws, Eqs. (4.1a) and (4.1b). We start in Section 4.2 with the case of pressurized rings and then continue to the case of particle-encapsulating rings in Section 4.3. Results of the simulations and their relation to the analysis by Fisher *et al.* is discussed in Section 4.4.

#### 4.2 Swelling of Pressurized Rings

In order to test the scaling conjecture, Eq. (4.1a), we follow the model and Monte Carlo scheme presented by Fisher and coworkers for a 2D self-avoiding envelope subject to an inflating pressure difference p [25, 73, 74]. The manifold is represented by a closed chain of N self-avoiding circles (beads) of diameter 2a = (5/9)l, linked by tethers of maximum length  $l \equiv 1$ . In each MC step every bead is moved to a random position within a square of  $(-0.4a, 0.4a)^2$  about its former position. These values of a, 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 to 800.

The mean volume of the ring as a function of pressure difference is presented in Fig. 4.1. The different data sets collapse onto a single curve once the mean volume is rescaled by the maximum volume of the ring,  $V_{\text{max}} = N^2/(4\pi)$ , and the pressure by  $N^{-1}$ , in accord with Eq. (4.1a). The scaling law, however, yields a vanishing mean volume for p = 0, whereas the unperturbed ring has a finite mean volume,  $V_0 \sim N^{2\nu}$ ,  $\nu = 3/4$ . In the thermodynamic limit  $(N \to \infty)$  the correction is negligible,  $V_0/V_{\text{max}} \sim N^{-1/2} \to 0$ , but for finite rings the scaling of Eq. (4.1a) must break down for sufficiently small p, as seen in Fig. 4.1. (The value of  $V_0$  was directly measured from the simulations.) Therefore, to capture the linear dependence of  $\langle V \rangle$  on p, as predicted by Eq. (2.5a) for d = 2 and  $\nu = 3/4$ , we replot the data for  $\langle V \rangle - V_0$  in the inset of Fig. 4.1. 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.



Figure 4.1: 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. (4.1a),  $V_{\text{max}} = N^2/(4\pi)$  being the maximum volume of the ring. 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.

#### 4.3 Swelling of Particle-Encapsulating Rings

We proceed to the scenario of particle-encapsulating manifolds by setting p = 0 and introducing Q ideal particles at random positions within the vesicle. Avoidance is imposed between the particles and envelope beads (but not between the particles themselves), with particle-bead minimum distance of 2a. The MC step is extended to include repositioning of each particle within a square of  $(-0.4a, 0.4a)^2$  about its former position. This maximum step size, together with avoidance between particles and envelope beads, and maximum tether length, ensure that particles are forever trapped in the ring. Rings of N = 50 to 800 have been simulated, with Q ranging between 0 and 20N.

In Fig. 4.2 we present the mean volume as a function of Q. In accordance with Eq. (4.1b) all data collapse onto a single curve once  $\langle V \rangle$  is rescaled by  $N^2$  and Q by N. Here, as in the case of fixed p discussed above, scaling breaks as  $Q \to 0$ , when  $\langle V \rangle$  becomes affected by the finite volume of the unperturbed state. The power law predicted by Eq. (2.5b) for 2D self-avoiding rings,  $\langle V \rangle \sim V_{\max}(Q/N)^{1/2}$ , is nevertheless



Figure 4.2: 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. (4.1b),  $V_{\text{max}} = N^2/(4\pi)$  being the maximum volume of the ring. Also plotted are the data points from the fixed-p simulation (Fig. 4.1), whose horizontal coordinate is calculated as  $p\langle V(p)\rangle/N$ . 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 1/2 is shown for reference.

verified after subtracting  $V_0$  from the mean volume (Fig. 4.2 inset).

To check the equivalence of the fixed-p and fixed-Q scenarios for this system we transform the data for pressurized rings (Fig. 4.1) according to  $Q(p) = p\langle V(p) \rangle$ , as is appropriate for an ideal gas (recall that  $k_{\rm B}T \equiv 1$ ), and present them in Fig. 4.2 alongside the data for fixed Q. The data sets of the two scenarios match nicely over the entire ranges of p and Q.

#### 4.4 Discussion

We have seen in this chapter an example of a model vesicle which shows gradual swelling in both the fixed-p and fixed-Q ensembles. In accord with the blob analyses of Chapter 2, for the current values of d and  $\nu$  the scaling laws Eqs. (2.6a) and (2.6b) (or, alternatively, Eqs. (4.1a) and (4.1b)) hold throughout the swelling (*i.e.*, for all values of p or Q) with no criticality. In this case there is a single-valued smooth transform from one ensemble to the other, which is obtained by replacing p with  $Q/\langle V \rangle$  (for an ideal gas). This is indeed verified in Fig. 4.2 where the mean volume of pressurized rings is plotted as a function of  $p\langle V(p)\rangle/N$ . The data collapse convincingly on the simulations of the fixed-Q ensemble.

Unlike the analysis of Fisher *et al.*, which holds also for the unperturbed state but does not capture the smooth state, our scaling conjecture breaks when the perturbation vanishes, but holds for highly swollen vesicles. Nevertheless, in the selected thermodynamic limit, *i.e.*,  $p \to 0$  and  $N \to \infty$  such that pN is finite, our scaling holds *throughout* the swelling and breaks only for  $pN \leq N^{-1/2} \to 0$ .

Obviously, the swelling of 2D envelopes studied here and in the preceding chapter is of idealized systems. Our goal has been to demonstrate the validity and power of the scaling predictions and examine the fundamental issue of ensemble (in)equivalence. Possible implications for more realistic systems of unconstrained volume, e.g., a threedimensional fluid vesicle, are presented in the following chapters.

# Chapter 5 Swelling of 3D Fluid Vesicles

Having considered in Chapters 3 and 4 somewhat artificial two-dimensional random manifolds, we turn in this chapter to a more realistic model system — that of a three-dimensional fluid vesicle. According to the general scaling analysis of Chapter 2 no criticality emerges for d > 2, neither for pressurized nor for particle-encapsulating vesicles. Nevertheless, the statistics of the specific model treated below is inconsistent with the scaling analysis assumptions. Here we present a different analysis appropriate for this model. It is shown that for weakly swollen particle-encapsulating vesicles the mean volume is linearly dependent on the number of trapped particles, implying (according to Section 2.3) a criticality of pressurized vesicles. Both results are confirmed by Monte Carlo simulations of 3D fluid manifolds. For pressurized vesicles a first-order transition from deflated branched-polymer-like phase to a swollen one is found, as previously reported [78]. Above the transition point, our simulation data scale according to Eq. (2.6a). For particle-encapsulating vesicles the simulations reveal, for small number of particles, a linear dependence of the volume on particle number. The data throughout the swelling follow a single scaling law in agreement with Eq. (2.6b).<sup>1</sup>

<sup>&</sup>lt;sup>1</sup>The results presented in this chapter were published in Ref. [70].

#### 5.1 Introduction

In this chapter we turn to a slightly more realistic three-dimensional model of a fluid vesicle. The model was extensively studied by MC simulations under fixed pressure difference p [77, 78, 79, 80, 81, 59, 82]. reduce cites The vesicle is represented by a closed, triangulated, off-lattice network of N nodes (self-avoiding spheres) of diameter  $2a = l/\sqrt{2}$ , interconnected by a fixed number N of tethers of maximum length  $l \equiv 1$ . (See Section 1.2.3.) 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  $(-0.2a, 0.2a)^3$  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 performed 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). See visual example in Fig. 5.1. This move is weighted as well by a factor of  $e^{p\Delta V}$ , where  $\Delta V$  is the volume change due to this construction. The choice of a, l, passing through another part of the network, making the manifold self-avoiding.



Figure 5.1: Changing the envelope connectivity. A tether that is common to two triangles is cut and reattached to the other two nodes.

The swelling of this model vesicle as a function of p follows three regimes [77]:

- (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 ⟨V⟩ ~ R<sup>2</sup> ~ N, with negligible dependence on p [77, 63, 114, 115].
- (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  $\langle V \rangle \sim p^{0.47} N^{1.73}$  [77].

(iii) At sufficiently large p the power-law behavior of (ii) crosses over to asymptotic swelling toward the maximum volume.

The scaling conjectures of Chapter 2 [Eqs. (2.6a) and (2.6b)] predict continuous swelling in both the fixed-p and fixed-Q cases with

$$\langle V \rangle = N^{3/2} f_p(p N^{1/2}),$$
 (5.1a)

$$\langle V \rangle = N^{3/2} f_Q(Q/N).$$
 (5.1b)

Yet, the blob analysis presented in Section 2.2 obviously fails in regime (i) of low swelling, since the volume enclosed in such collapsed manifolds does not follow the standard relation  $\langle V \rangle \sim R^d$ . In this chapter we introduce, therefore, an alternative scaling analysis for this regime and further investigate the swelling as a function of p and Q using Monte Carlo simulations (Secs. 5.2 and 5.3 respectively). Conclusions reached throughout the investigation are further discussed in Section 5.4.

#### 5.2 Swelling of Pressurized Vesicles

In this section we investigate the swelling of the model system described above due to an inflating pressure difference. We begin by introducing an alternative blob analysis to that presented in Chapter 2 for the low swelling regime. In this collapsed state 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 [116],  $\sigma \sim 1$  (in units of  $k_{\rm B}T/l^2$ ). Applying Laplace's law,  $p \sim \sigma/R \sim N^{-1/2}$ , we find that regime (i) occurs for  $p \leq N^{-1/2}$ , *i.e.*,

$$p \lesssim N^{-1/2}$$
:  $\langle V \rangle \simeq V_0 \sim N.$  (5.2a)

In regime (ii) the scaling analysis of Chapter 2 should hold. Comparison of the previously obtained power law,  $\langle V \rangle \sim p^{0.47} N^{1.73}$ , with Eq. (2.5a) for d = 3, gives a swelling exponent  $\nu = 0.787$  [77].

We note that the scaling analysis as previously presented for this model [78, 80, 82]

was inconclusive as to how p should scale with N. For example, the dependence of the critical pressure  $p^*$  on N has been controversial [59], ranging between  $N^{-0.5}$  [78] and  $N^{-0.69}$  [82].<sup>2</sup> Our modified scaling analysis [Eqs. (2.5a) and (2.6a), resulting in Eq. (5.1a)] indicates that p scales with  $N^{-1/2}$ . The scaling argument for  $p > p^*$ , together with Eq. (5.2a) for  $p < p^*$ , strongly suggest that  $p^* \sim N^{-1/2}$ .<sup>3</sup> This will be supported by MC simulations below.

We have repeated the MC simulations for fixed p, as presented in Ref. [77], while extending them to larger vesicles and higher pressure values. The results are shown in Fig. 5.2, scaled according to Eq. (5.1a). 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  $p \gtrsim p^*$  is not inconsistent with the power law of Ref. [77] and Eq. (2.5a) with  $\nu$  between 0.7 and 0.8 (Fig. 5.2 inset), yet this power-law regime is too narrow to be clearly resolved.

#### 5.3 Swelling of Particle-Encapsulating Vesicles

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

$$Q/\langle V \rangle \lesssim N^{-1/2}: \quad \langle V \rangle \sim N^{3/2}(Q/N).$$
 (5.2b)

(We have seen in Section 2.3 that such a linear dependence of  $\langle V \rangle$  on Q is intimately related to the phase transition observed as a function of p.) The scaling law of Eq. (5.2b) for the low-swelling regime turns out to be in line with that of Eq. (2.5b). Hence, despite the inadequacy of the blob analysis in regime (i), we expect the scaling conjecture, Eq. (5.1b), 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 radius a, randomly positioned inside the vesicle. The particles do not interact with each other but have a hard-core repulsion with the network nodes, thus keeping them trapped inside the vesicle. The MC step is extended

<sup>&</sup>lt;sup>2</sup>Plaquette models (see Section 1.2.3) of closed surfaces subject to a pressure difference reveal a similar phase transition [65, 117]. However, the transition occurs at  $p^* \sim N^{-1}$  [65].

<sup>&</sup>lt;sup>3</sup>Similarly, the critical pressure in 2D Gaussian and freely jointed rings was analytically found in Chapter 3 to scale as  $N^{-1/(d-1)} \sim N^{-1}$ .



Figure 5.2: 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 is scaled according to Eq. (5.1a), exhibiting a discontinuous transition at  $p^* \sim N^{-1/2}$ . For  $p > p^*$  the data collapse onto a single curve. Inset presents the same data for  $p > p^*$  on a log–log scale, the solid line having a slope of 0.6 (corresponding to  $\nu = 0.75$ ).

to include random repositioning of each particle within a cube of  $(-0.2a, 0.2a)^3$  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. 5.3. Once the volume  $V_0$  of the unperturbed (branched) state [Eq. (5.2a)], which is inaccessible to the particles due to their excluded-volume interaction with the manifold, is subtracted from  $\langle V \rangle$ , the data collapse according to Eq. (5.1b). Two power-law regimes are seen in Fig. 5.3 (inset). At low swelling  $\langle V \rangle$  increases linearly with Q, in agreement with Eq. (5.2b).<sup>4</sup> At about  $Q \simeq 0.08N$  the swelling crosses over to a different power law which, when fitted to Eq. (2.5b), yields  $\nu = 0.75(2)$ . This value is close to that found in fixed-p simulations,  $\nu = 0.787$  [77].<sup>5</sup> For larger values

<sup>&</sup>lt;sup>4</sup>Artificially attempting to extract  $\nu$  for the low-swelling regime by fitting these results to Eq. (2.5b), 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 above.

<sup>&</sup>lt;sup>5</sup>We note that this value of  $\nu$  is also suspiciously close to the one known for self-avoiding polymerized (*i.e.*, solid) 3D manifolds,  $\nu \simeq 0.8$ . (See, *e.g.*, Section 1.2.2 and Ref. [60].) This suggests that the configurations of the variable-connectivity (fluid) manifold studied here, when it is suffi-

of Q this power-law regime should cross over to the asymptotic saturation toward maximum volume. Because of computer limitations we could sample only the lowest edge of this regime (Fig. 5.3 inset).



Figure 5.3: 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 according to Eq. (5.1b) once the volume of the unperturbed vesicle,  $V_0 \sim N$ , is subtracted from  $\langle V \rangle$ . Inset represents the same data on a log-log scale, exhibiting a linear regime for  $Q \ll N$ ,  $(\langle V \rangle - V_0)/N^{3/2} \sim (Q/N)^{1.02(3)}$  (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  $Q \simeq 0.08N$ .

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 ([77] and Fig. 5.4A), *i.e.*, coexistence of collapsed and swollen states, for particle-encapsulating vesicles we obtain unimodal distributions for all values of Q (Fig. 5.4B).

Finally, let us consider the effective pressure exerted by the encapsulated ideal particles,  $p = Q/\langle V \rangle$ . From Eq. (5.1b) we have

$$p = N^{-1/2} \psi(Q/N), \quad \psi(x) = x/f_Q(x).$$
 (5.3)

ciently swollen, may become statistically equivalent to those of polymerized membranes. However, we currently cannot prove this suggestion.



Figure 5.4: Volume distribution functions of a 362-nodes vesicle. In panel A the bimodal distribution obtained in the fixed-p case at the transition point [77] is plotted for reference. In panel B a unimodal distributions appears for all values of Q.

In the low-swelling regime we have found a linear behavior,  $f_Q(x \ll 1) \sim x$ , [Eq. (5.2b) and Fig. 5.3 inset]. Thus,  $\psi(x \ll 1) = \text{const}$ , *i.e.*, the effective pressure does not change with Q throughout this regime! Figure 5.5 demonstrates the data collapse according to Eq. (5.3), as well as the finite, constant pressure  $p_{\min}$  at low swelling even for the smallest values of Q. (In calculating the concentration or pressure from the simulations we have considered the particle-accessible volume,  $V - V_0$ .) One expects  $p_{\min}$  to coincide with the transition value under fixed pressure,  $p^*$ . (Compare also Fig. 5.4A, plotted for  $p = p^*$ , with Fig. 5.4B, where the effective pressure stays essentially constant at  $p_{\min}$  for all curves.) We find, however,  $p^* \simeq 1.8p_{\min}$ . 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.

#### 5.4 Discussion

In this chapter we have investigated a model of three-dimensional fluid vesicles. As predicted by the scaling analysis of Chapter 2, the swelling of particle-encapsulating vesicles is continuous with no criticality and obeys a single scaling law, Eq. (5.1b) (see Fig. 5.3). By contrast, the swelling of pressurized vesicles undergoes a first-order transition from a deflated branched-polymer-like phase to a more swollen one. Unlike the criticality of 2D freely-jointed, pressurized rings, as studied in Chapter 3, the



Figure 5.5: Effective pressure of encapsulated particles as a function of particle number. Data have been obtained from MC simulations for vesicles of various sizes N and rescaled according to Eq. (5.3). The arrow indicates the crossover between the two swelling regimes at  $Q \simeq 0.08N$ .

one described in this chapter for 3D pressurized vesicles could not be foreseen by the general blob analysis of Chapter 2. This criticality stems from the unusual (collapsed) behavior of this model in the low-swelling regime. Nevertheless, taking into account this behavior, we have reached a modified scaling argument for the weak-swelling regime, which is linear in Q, implying, indeed, a criticality with p. Furthermore, for p larger than the critical pressure  $p^*$ , the swelling obeys a single scaling law, Eq. (5.1a), as predicted by the general scaling analysis of Chapter 2 (see Fig. 5.2).

As a final comment on an issue that has not been addressed in this work, we note that extending the fixed-p scenario to include a surface bending rigidity  $\kappa$  leads to the removal of the first-order transition above a certain value of  $\kappa$  [81].

## Chapter 6

# Critical Behavior of Highly Swollen Particle-Encapsulating Vesicles

In Chapters 3–5 we have considered the effect of pressure difference and trapped particles on strongly fluctuating, random manifolds. By contrast, in this chapter we consider a realistic, ubiquitous scenario where a smooth semipermeable vesicle is embedded in solution while enclosing a fixed number of solute particles. Assuming that the vesicle has a maximum volume, we show that its swelling with increasing number of trapped particles (or decreasing concentration of the outer solution) exhibits a continuous phase transition from a fluctuating state to the maximum-volume configuration. Beyond the transition vesicle fluctuations are suppressed and appreciable pressure difference and surface tension build up. This criticality is unique to particle-encapsulating vesicles, whose volume and inner pressure both fluctuate, and is absent when the swelling is caused by a controlled pressure difference. In practice, the transition is expected to be followed by membrane rupture (lysis). The criticality implies a universal swelling behavior of vesicles as they approach their limiting volume and osmotic lysis. The chapter deals with the system on a general thermodynamic level, and the results are insensitive to the particular microscopic description of the vesicle and the encapsulated solution.<sup>1</sup>

<sup>&</sup>lt;sup>1</sup>The results presented in this chapter were published in Ref. [118].

#### 6.1 Introduction

In Chapter 1 we have described the nature of membrane vesicles as well as several approaches to study them (Sections 1.2.1 and 1.2.2). Using these approaches the elasticity and statistical mechanics of the membrane were addressed under various constraints, such as area and enclosed volume (*e.g.*, Refs. [48, 51, 119, 120]), or area and pressure difference across the membrane [121, 122, 59], yielding various shapes and shape transformations. Actual vesicles are always immersed in solution and thus contain solvent (water) as well as solute. Since the bilayer membrane contains a hydrophobic core, the permeation of both water and solute molecules is hindered, and over sufficiently short time, therefore, the vesicle volume is fixed. Yet, since permeation rates of solute molecules are orders of magnitude lower than that of water (see, *e.g.*, Section 1.2 or Ref. [37]), at sufficiently long times, typically a few seconds, most vesicles are found in a wide semipermeable regime, where water can be considered as exchanged between the interior and exterior, while the solute remains trapped inside.

As a result, it has been assumed that the exterior solution concentration and number of encapsulated particles determine the vesicle volume in practice [48, 51, 119] the mean volume adjusts through water permeation so as to annul the osmotic pressure difference across the membrane, thus avoiding an extensive free energy penalty. This scenario has been experimentally verified [83] and utilized to measure membrane permeabilities of various solutes [37] and create osmotic motors [84]. Volume fluctuations around the osmotically determined mean value have been considered as well [123]. However, at high swelling, as the vesicle approaches its maximum volume, this volume-adjustment description must break down, and appreciable pressure difference and surface tension will begin to build up. Further swelling eventually leads to pore formation and osmotic lysis [34, 124, 125]. The change in swelling behavior from small to appreciable pressure difference and surface tension, in particular, whether it is a smooth crossover or a sharp transition, is the focus of the current chapter.

#### 6.2 Model

We describe the vesicle as a closed surface composed of N molecules and having maximum volume  $V_{\text{max}} \sim N^{3/2}$ . It is assumed that at  $V_{\text{max}}$  the vesicle has a nonextensive number of configurations. The vesicle encloses Q solute particles, which do not directly interact with the surface other than being trapped inside it. The vesicle is immersed in a solution of fixed concentration and temperature, which exerts an outer osmotic pressure  $p_0$  on the membrane. Since solvent molecules are exchanged between the interior and exterior, the vesicle volume is not specified and, hence, neither are its inner particle concentration and pressure. Thus, the partition function of the system involves integration over all possible volumes,

$$\mathcal{Z}(T, p_{\rm o}, Q, N) = \int dV Z_{\rm v}(T, V, N) Z_{\rm s}(T, V, Q) e^{-p_{\rm o} V/(k_{\rm B}T)}, \tag{6.1}$$

where  $Z_{\rm v}$  and  $Z_{\rm s}$  are the canonical partition functions of the vesicle and solute particles, respectively, for a given volume V. The thermal energy  $k_{\rm B}T$  is hereafter set to unity. For the solute we write

$$Z_{\rm s} = e^{-QF_Q(Q/V)},\tag{6.2}$$

where  $F_Q$  is the canonical free energy per solute molecule.

A key issue for the highly swollen vesicles studied here is how  $Z_v$  behaves as V approaches  $V_{\text{max}}$ . It is shown below that, quite generally,

$$Z_{\rm v}(V \lesssim V_{\rm max}) \sim (V_{\rm max} - V)^{\eta N},\tag{6.3}$$

where  $\eta$  is a coefficient of order unity. This result readily follows from the two requirements, that (i) the vesicle free energy be extensive in N for  $V < V_{\text{max}}$ , and (ii) the probability density function of vesicle volumes vanish at  $V_{\text{max}}$ .

A more detailed argument goes as follows. To find  $Z_v$  we should integrate over all surface configurations the factor  $e^{-H[\mathcal{R}]}\delta(V-V[\mathcal{R}])$ , where  $V[\mathcal{R}]$  is the volume of configuration  $\mathcal{R}$ , and  $H[\mathcal{R}]$  its energy (including, *e.g.*, contributions from bending rigidity and surface interactions). For  $V \simeq V_{\text{max}}$  one can generally represent the configurations by the amplitudes  $\{u_n\}$  of N normal modes. (For example, in the case of nearly spherical vesicles these modes are spherical harmonics [51, 127, 128]; see also Appendix C.) One then expands  $V[\mathcal{R}]$  to second order around the maximum volume,

$$V[\mathcal{R}] \simeq V_{\max} - \sum_{n} C_n |u_n|^2.$$
(6.4)

Assuming that H is nonsingular at  $V_{\text{max}}$ , and using the integral representation of the

delta function, we get

$$Z_{\rm v} \sim e^{-H(V_{\rm max})} \int d[u_n] dp \exp[ip(V_{\rm max} - V - \sum C_n |u_n|^2)].$$
(6.5)

Integration over the amplitudes gives a factor of  $p^{-1/2}$  per mode which, upon integration over p, yields Eq. (6.3) with  $\eta = 1/2$ . Thus, provided that N is the number of independent modes, we always have  $\eta = 1/2$ . Since accurately relating the number of molecules with the number of modes while considering all constraints may not always be straightforward, we keep a general value of  $\eta$  in the formulation.

We have rigorously derived the partition function  $Z_v$  for two specific cases — 2D freely-jointed rings and nearly spherical 3D vesicles. In the 2D case we present two different derivations in Appendices B and D, and the calculation for the 3D case is given in Appendix C. All these results are in agreement with the aforementioned general prediction, *i.e.*, Eq. (6.3) with  $\eta = 1/2$ .

#### 6.3 Results

Substituting Eqs. (6.2) and (6.3) in Eq. (6.1) while specifying the solute free energy  $F_Q$ , one can perform the integration over V for given Q,  $p_o$ , and N. In Fig. 6.1 we present the resulting mean volume,  $\langle V \rangle = -\partial \ln \mathcal{Z} / \partial p_o$ , as a function of Q for the case of an ideal solution,  $F_Q(Q/V) = \ln(Q/V) - 1$ . As N is increased,  $\langle V \rangle$  is seen to approach a critical behavior (a discontinuous first derivative) at  $Q_c = p_o V_{\text{max}}$ .

We now proceed to investigate this criticality analytically for a general (nonideal) solution. The partition function can be rewritten as  $\mathcal{Z} \sim \int dV e^{-F}$ , with

$$F = -\eta N \ln(V_{\rm max} - V) + Q F_Q(Q/V) + p_{\rm o} V.$$
(6.6)

Minimizing F with respect to V and applying a first-order saddle-point approximation for the integral (which is equivalent to a mean-field assumption), we obtain the following equation for  $\langle V \rangle$ :

$$Q^{2}F_{Q}'(Q/\langle V\rangle)/\langle V\rangle - p_{\rm o}\langle V\rangle = \eta N\langle V\rangle/(V_{\rm max} - \langle V\rangle).$$
(6.7)



Figure 6.1: Order parameter M as a function of control parameter t for the case of an ideal solution encapsulated in vesicles of various sizes. Solid curves show the mean-field results [Eq. (6.8)], while dotted curves are obtained from numerical integration of the full partition function [Eq. (6.1)]. Datasets from top to bottom (bottom to top in the inset), correspond to  $p_{\rm o} = 1$ , N = 30 (green);  $p_{\rm o} = 1$ ,  $N = 10^3$  (blue);  $p_{\rm o} = 5$ ,  $N = 10^3$  (indigo);  $p_{\rm o} = 1$ ,  $N = 10^5$  (red); and the  $N \to \infty$  limit [Eq. (6.9), black]. Only for the smallest vesicle size (N = 30) are the mean-field and numerical results distinguishable. Inset shows rescaled data according to Eq. (6.11), where the uppermost curve (solid black) is the theoretical scaling function. The values  $\eta = 1/2$  and  $V_{\rm max} = N^{3/2}a^3$  have been used in all datasets, and  $p_{\rm o}$  is given in units of  $k_{\rm B}T/a^3$ , a being an arbitrary unit length.

Expansion in  $V_{\text{max}} - \langle V \rangle$  yields for our order parameter,  $M = 1 - \langle V \rangle / V_{\text{max}}$ ,

$$M = \left[\sqrt{[s-t(q)]^2 + 4sg(q)} - s - t(q)\right] / (2g(q))$$
(6.8)

$$\xrightarrow{N \to \infty} (|t| - t)/(2g), \tag{6.9}$$

where  $q = Q/V_{\text{max}}$  is the solute concentration at  $V = V_{\text{max}}$ ,  $t(\rho) = [\rho^2 F'_Q(\rho)/p_o - 1]$ is the rescaled difference between the solute pressure at concentration  $\rho$  and the outer pressure  $[t(\rho = q)$  acting as the control parameter of the transition],  $s = \eta N/(p_o V_{\text{max}}) \sim N^{-1/2}$ , and  $g(q) = q^2 [2F'_Q(q) + qF''_Q(q)]/p_o > 0.^2$ 

Equations (6.8) and (6.9) describe a continuous phase transition at  $q = q_c$  which solves the equation  $t(q_c) = 0$ , *i.e.*, for which the inner pressure would just balance the

<sup>&</sup>lt;sup>2</sup>The function  $g(\rho)$  is proportional to the derivative of the solute chemical potential with respect to Q, which is strictly positive (assuming a solution far from condensation).

outer one if the volume were equal to  $V_{\text{max}}$ . The parameter  $t(\rho = q)$  is related to the actual control parameter, Q or q, via the solute equation of state, *i.e.*, the specific choice of  $F_Q$ . In the simple example of an ideal solution,  $F_Q(Q/V) = \ln(Q/V) - 1$ , the critical point is at  $q_c = p_o$  (*i.e.*,  $Q_c = p_o V_{\text{max}}$ ), and we have  $t = Q/Q_c - 1$  and g = 1. The transition occurs in the region  $|t| \leq \Delta = (4sg)^{1/2} \sim p_o^{-1/2} N^{-1/4}$ , along which M crosses over from finite values to very small ones,

$$M = \begin{cases} -t/g \sim N^0 |t|^1 & t \ll -\Delta \\ \Delta/(2g) \sim N^{-1/4} |t|^0 & |t| \ll \Delta \\ \Delta^2/(4gt) \sim N^{-1/2} t^{-1} & t \gg \Delta. \end{cases}$$
(6.10)

In the thermodynamic limit,  $N \to \infty$ , this crossover turns into a sharp corner [Eq. (6.9)], *i.e.*, a discontinuity in the first derivative of M with respect to t. From Eq. (6.8) we find also that M follows a scaling law within the transition region,

$$M/\Delta = g^{-1}\tilde{M}(t/\Delta), \quad \tilde{M}(x) = (\sqrt{x^2 + 1} - x)/2,$$
 (6.11)

which is verified in Fig. 6.1 (inset). In addition, we calculate from Eq. (6.11) the compressibility,  $\chi = \partial M / \partial p_o$ ,

$$\chi = (gp_{\rm o})^{-1} \tilde{\chi}(t/\Delta), \quad \tilde{\chi}(x) = (1 - x/\sqrt{x^2 + 1})/2.$$
 (6.12)

Performing the next-order saddle-point calculation (*i.e.*, including fluctuations beyond mean field) yields negligible corrections to M, of order  $N^{-3/2}$ ,  $N^{-5/4}$ , and  $N^{-1}$ , respectively, in the three domains of Eq. (6.10). Thus, the mean-field description is accurate, as is also confirmed by numerical integration of the partition function (Fig. 6.1).

Equation (6.7) (upon division by  $\langle V \rangle$ ) is just the Laplace law, balancing the pressure difference across the membrane (left-hand side) with a surface term (right-hand side). We therefore identify the pressure difference and surface tension as

$$\Delta p = (\eta N / V_{\text{max}}) M^{-1} \sim N^{-1/2} M^{-1},$$
  

$$\sigma \sim R \Delta p \sim M^{-1},$$
(6.13)

where  $R \sim N^{1/2}$  is the vesicle radius. Thus,  $\Delta p$  and  $\sigma$  change from negligible values

below the transition to appreciable ones above it. Specifically,  $\Delta p$  is of order  $N^{-1/2}$ ,  $N^{-1/4}$ , and 1, while  $\sigma \sim 1$ ,  $N^{1/4}$ , and  $N^{1/2}$ , below, at, and above the critical point, respectively.

#### 6.4 Discussion

Since Eqs. (6.1)–(6.3), which underly the entire analysis, contain no microscopic information, the model is purely thermodynamic, in the sense that any specific microscopic model for the vesicle and encapsulated solution (so long as the vesicle has a state of maximum volume and negligible entropy) should lead to the same results. This implies also that the continuous transition does not necessarily involve a divergent correlation length.<sup>3</sup>

We have checked these statements for the specific example of a nearly spherical envelope of N nodes and fixed total area  $4\pi R_0^2$ , enclosing an ideal solution. See Appendix C. (The two-dimensional analogue is considered in Appendix D.) The vesicle shape is defined in this case by  $R(\theta, \varphi)$ , the distance of the membrane from the center as a function of solid angle, whose deviation from  $R_0$  can be decomposed into spherical harmonics,  $R(\theta, \varphi) = R_0 [1 + \sum_{l=0}^{l_{\max}} \sum_{m=-l}^{l} u_{lm} Y_{lm}(\theta, \varphi)]$ , where  $(l_{\max} + 1)^2 = N$ . Integration of the resulting partition function over the amplitudes  $u_{lm}$  within a saddlepoint approximation recovers Eqs. (6.8)–(6.12). In addition, we have calculated for this case the correlation function [Eq. (C.12)],

$$\langle u_{lm}u_{l(-m)}\rangle \sim \frac{M}{N} \frac{1}{l(l+1)-2}, \qquad l > 1,$$
 (6.14)

which exhibits a critical suppression of amplitude but no divergent correlation length. Expectedly, this fluctuation spectrum is identical to that of a spherical membrane with surface tension  $\sigma \sim M^{-1}$ , in accord with Eq. (6.13).

Equations (6.11) and (6.12) characterize the sharpening of the transition with increasing system size. If we recast them in the form of finite-size scaling using the conventional critical exponents [26],  $M \sim R^{-\beta/\nu^*} \tilde{M}(R^{1/\nu^*}t)$  and  $\chi \sim R^{\gamma/\nu^*} \tilde{\chi}(R^{1/\nu^*}t)$ , we readily extract  $\beta = 1$ ,  $\gamma = 0$ , and  $\nu^* = 2$ . The values of  $\beta$  and  $\gamma$  are consistent with

 $<sup>^{3}</sup>$ Criticality without a divergent correlation length has been found in other mean-field transitions, *e.g.*, Ref. [129].

the linear increase of M below the transition [Eq. (6.9) and Fig. 6.1]. Notwithstanding the absence of a divergent correlation length, one can use  $\nu^*$  to define a length scale,  $\xi \sim |t|^{-\nu^*}$ , such that the system lies in the critical domain if  $R < \xi$ . The divergent  $\xi$  does not relate to correlations but to the competition between surface degrees of freedom ( $\sim N$ ) and three-dimensional ones ( $\sim N^{3/2}$ ). This competition determines the width of the transition,  $\Delta \sim [N/(p_0 V_{\text{max}})]^{1/2}$ , making it shrink with increasing N. Repeating the analysis for a ring in two dimensions yields a similar mean-field transition with identical exponents. We are not aware of another transition whose mean-field limit has the exponents found above.<sup>4</sup>

The phase transition just characterized is a unique feature of particle-encapsulating vesicles. Specifically, it is a consequence of the effective inner pressure being dependent on the volume (through  $F_Q(Q/V)$  for fixed Q), while the latter fluctuates. This leads to pressure difference and surface tension which are nonanalytic in Q [Eq. (6.13)] and a consequent breaking of the equivalence between the fixed-pressure (or fixed-tension) scenario and that of fixed Q. Indeed, if the enclosed solution is replaced with a given inner pressure  $p_i$  (*i.e.*, upon substituting in Eq. (6.1)  $Z_s = e^{p_i V/T}$ ), it is straightforward to show that  $M = \eta N[(p_i - p_o)V_{\text{max}}]^{-1}$ , in agreement with Eq. (6.13). (We have obtained the same result in Chapter 3 as an exact asymptote for highly swollen freely-jointed ring; see Eq. (3.27).) Therefore, in the case of a given pressure difference (or tension) the vesicle swells gradually with  $p_i$  (or  $\sigma$ ) without criticality.

Furthermore, the introduction of a diffusive contact with a particle reservoir,<sup>5</sup> *i.e.*, replacing the particle-number constraint with a chemical potential, is equivalent (via the solute equation of state) to specifying the inner pressure. Hence, there is no criticality in the grand-canonical case either, and the two ensembles are manifestly not equivalent. (One may refer to Section 3.3 for the case of 2D freely-jointed rings in the grand-canonical ensemble. In this case we have explicitly demonstrated that fixing the chemical potential is thermodynamically equivalent to fixing  $p_i$ , and both

<sup>&</sup>lt;sup>4</sup> Note that the exponents violate the hyperscaling relation,  $2\beta + \gamma = d\nu^*$  (*d* being the dimensionality). This so-called breakdown of finite-size scaling, known in other mean-field transitions, is related to the appearance of the divergent length  $\xi$ , which is not a correlation length. See *e.g.*, Refs. [130, 131].

 $<sup>{}^{5}</sup>$ We do not consider here diffusion of particles across the membrane, because this will entail a vanishing pressure difference. One may envisage instead a diffusive contact with a distant buffer.

scenarios are inequivalent to the case where the number of trapped particles is fixed.)

Another noteworthy limit is that of a pure solvent outside the vesicle,  $p_0 \rightarrow 0$ . The current analysis yields in this limit  $Q_c \rightarrow 0$  and  $\Delta \rightarrow \infty$ , *i.e.*, the transition disappears. What physically happens in this case, as was derived and obtained in Chapters 2–5, is that the swelling of the vesicle toward its maximum volume occurs already for much smaller particle numbers Q, scaling with the area N rather than the volume. (See, *e.g.*, the discussion in Chapter 2 after Eq. (2.5b).)

We have found that membrane vesicles, under rather general conditions, should behave critically as the number of solute particles encapsulated in them is increased or, equivalently, the outer osmotic pressure is decreased. It should be possible to experimentally observe this new phase transition, for example, by creating vesicles and subsequently diluting the outer solution in a controlled manner, or by using isotonic solutions of molecules with different membrane permeabilities [125, 126].

We mention three points relating to such an experiment. First, it should cover such time scales that the vesicle could be considered permeable to water. This can be sensitively controlled if water (aquaporin) channels [43, 44] are incorporated in the membrane, yet common lipid vesicles are also found in this regime over readily accessible time scales of a few seconds [83, 84, 125, 126].

Next we examine the assumption of a sharply defined maximum volume. One definition of  $V_{\text{max}}$  would be the volume enclosed by an unstretchable vesicle of a given area once out-of-plane fluctuations have been completely suppressed.<sup>6</sup> This assumption should be relaxed when the magnitude of in-plane (stretching) fluctuations becomes comparable to that of transverse ones. Since, for a tense membrane, the mean-square fluctuations of both modes have the same (quadratic) dependence on wavenumber, this crossover will occur simply when the surface tension,  $\sigma \sim (k_{\rm B}T/a^2)M^{-1}$  (Eq. (6.13), *a* being a molecular size), becomes comparable to the membrane stretching modulus, which is typically of order 10<sup>2</sup> dyne/cm [41]. For  $a \sim 1$  nm this happens when  $M \leq 10^{-2}$ , *i.e.*, when the mean volume deviates from  $V_{\rm max}$  by less than 1%.

<sup>&</sup>lt;sup>6</sup>The general derivation of Eq. (6.3) does not depend on specific normal modes. Hence, in principle, the analysis still holds in the case of combined transverse and in-plane fluctuations. One may define  $V_{\text{max}}$  then as the volume at which nonlinear-elastic or plastic terms set in. However, since the membrane is expected to rupture close to this point, such an extended description does not seem experimentally useful.

Thus, we expect the transition from appreciable to small values of M, along with the corresponding scaling behavior, to be manifest well before stretching becomes important. Moreover, since lipid membranes can sustain an in-plane strain of only a few percent before rupturing [124], the crossover to stretching-dominated dynamics will be shortly followed by vesicle lysis [125, 126].

Third, because of the weak dependence of the predicted transition width on N,  $\Delta \sim p_o^{-1} N^{-1/4}$ , the observed behavior is not expected to be very sharp. A typical micron-sized vesicle has about  $N \sim 10^8$  molecules in its membrane, leading, for a 0.1M solution, to  $\Delta \sim 10^{-1}$  only. The criticality could be verified, nonetheless, by checking data collapse according to the universal scaling law, Eq. (6.11).

Thus, our assumptions concerning semipermeability, maximum volume, and large number of molecules do not rule out an experiment aimed at the predicted critical swelling. (The suppression of small fluctuations near the transition, however, may be hard to measure.) More generally, this study highlights the qualitatively different behavior of semipermeable, particle-encapsulating vesicles as compared to those having fixed volume or pressure as studied previously. Since most natural and industrial vesicles belong to this class of systems, their different behavior should be taken into account, particularly in cases of high swelling and osmotic lysis.

# Chapter 7 Summary and Conclusions

In this dissertation we have studied the thermodynamics of particle-encapsulating vesicles — a system which is abundant in nature as well as in industry. While former studies concentrated on vesicles of either fixed volume or a given pressure difference across their envelope, we address a different thermodynamic class defined by the surface area, temperature, number of encapsulated particles, and outer pressure, while no constraint is imposed on the volume. This new ensemble is suitable for describing vesicles encapsulating solute molecules, which cannot permeate out of the compartment, while solvent molecules can diffuse more rapidly through the membranal envelope. Thus, the vesicle has an unconstrained volume. This class, although it is the one most commonly encountered in practice, has not been studied in the past and, more importantly, is not necessarily equivalent to the other known ensembles. Throughout this thesis we have examined the swelling of vesicles subject to either a fixed pressure difference p or a fixed number Q of trapped particles, and clarified when the swelling scenarios are thermodynamically equivalent and when they are not.

The difference in swelling behavior of these two ensembles stems already from a general scaling analysis, presented in Chapter 2. This analysis indicates that the swelling of random manifolds due to a fixed pressure difference might exhibit a phase transition while that of particle encapsulating vesicles is always gradual. A closer examination of this analysis shows, however, that inequivalence occurs only for a 2D manifold whose unperturbed statistics is Gaussian or freely jointed (random-walk-like). These predictions of criticality and ensemble inequivalence are indeed confirmed in Chapter 3 for freely jointed rings. Another model system of fluid vesicles in 3D, which cannot be properly described by the general scaling analysis. of Chapter 2 also

shows inequivalence between the fixed-p and fixed-Q scenarios (Chapter 5).

Let us now extend the discussion of Chapter 2 by considering a general power-law swelling response to particle number,  $\langle V \rangle \sim Q^{\alpha}$ . Transforming to the fixed-p ensemble (for an ideal solution) we get  $p(Q) = Q/\langle V \rangle \sim Q^{1-\alpha}$ , and  $\langle V \rangle \sim p^{\alpha/(1-\alpha)}$ . Several observations readily 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 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 for fixed Q, *i.e.*, inequivalence of the two swelling scenarios. In this limit of 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 (cf. Fig. 5.5). Thus, criticality and inequivalent phase spaces come hand in hand. In the standard case where the blob analysis of Chapter 2 holds, we get from Eq. (2.5b)  $\alpha = d(1-\nu)/(d-1)$ , and the condition  $\alpha \leq 1$  is equivalent to  $d\nu \geq 1$ . In addition, we have 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 thermodynamic one,  $\alpha \leq 1$ . Hence, we conclude that for most systems, which obey the analysis of Chapter 2, case (ii) above, involving criticality and inequivalence, can occur only in 2D, *i.e.*, for d = 2 and  $\nu = 1/2$ . (Model systems corresponding to this case were studied in Chapter 3.)

All of these general conclusions are supported by the specific studied examples. A 2D self-avoiding ring (Chapter 4) is an example of case (i) above. It obeys the scaling analysis of Chapter 2 with d = 2,  $\nu = 3/4$ , *i.e.*,  $\alpha = 1/2$ . (The value of  $\alpha$ has been confirmed by simulations; see Fig. 4.2.) This system exhibits no criticality under fixed p, and the two ensembles have been shown to be equivalent (Fig. 4.2). The more interesting case (ii) has been encountered in three systems. Two examples are provided by Gaussian and freely jointed rings in 2D (Chapter 3). 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 (Chapter 5), for which the blob analysis of Chapter 2 fails, yet a linear dependence of  $\langle V \rangle$  on Q has been found, *i.e.*,  $\alpha = 1$  [Eq. (5.2b) and Fig. 5.3]. Indeed, under fixed p ([75, 77] and Chapter 3) all three manifolds undergo phase transitions.

The 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 the standard case, where the blob analysis of Chapter 2 is valid, one needs to know merely the dimensionality d and the statistics of the unperturbed manifold (the swelling exponent  $\nu$ ) to predict the qualitative swelling behavior. In other, exceptional cases (*e.g.*, the 3D fluid vesicle of Chapter 5) 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 pressure p that they exert on the manifold, as these two intensive variables are related via the particles' equation of state. (For example, in the case of ideal particles one simply has  $\mu = \ln p$ .) The inequivalence of the fixed-Q and fixed- $\mu$  ensembles has been directly proven for freely jointed 2D rings (Chapter 3).

Finally, in Chapter 6 we have studied a realistic, general model of a particleencapsulating vesicle, which is immersed in solution, *i.e.*, is subject to an external osmotic pressure. Considering a finite surface area we have identified a new continuous phase transition in which the vesicle changes from a fluctuating state to that of maximum volume. This result is general regardless of the microscopic model used for the vesicle or the solution. The criticality is removed when the constraint of fixed number of particles is replaced by a fixed internal pressure. The vesicle then reaches its maximum-volume configuration only asymptotically at  $p \to \infty$ . The continuous phase transition implies a universal behavior of particle-encapsulating vesicles as they swell toward their maximum volume and osmotic lysis.

In this thesis, a coherent unified theory of particle-encapsulating vesicles is presented. We have allowed ourselves to treat highly idealized manifolds at high temperatures, *i.e.*,  $l_{\rm p} \ll L$ , in order to infer and demonstrate the unique properties of this ubiquitous thermodynamic ensemble. In Chapter 6, by contrast, we have reached rather general and surprising predictions relevant to realistic, smooth ( $l_{\rm p} > L$ ), highly swollen particle-encapsulating vesicles. These predictions can be directly checked in experiments, which will hopefully be motivated by this work.

A possible extension to this work may treat semiflexible particle-encapsulating manifolds, *i.e.*, incorporating a bending rigidity  $\kappa$  to the studied model systems. For the case of fixed p, assuming a finite  $\kappa$  has already been considered [25, 80, 59, 76]. In the 2D case, introducing  $\kappa$  merely rescales the number of monomers and link length, and thus, does not change our qualitative results [76]. In particular, the criticality of the freely jointed case, described in Chapter 3, remains. However, for 3D fluid vesicles studied in Chapter 5, the criticality with p seems to disappear above some value of  $\kappa$  [80, 59]. The behavior of particle-encapsulating vesicles with a non-vanishing bending rigidity is yet to be explored. In particular, it will be interesting to check whether the highly universal picture achieved here (*i.e.*, a single scaling law for swelling with Q), will remain so after the addition of bending rigidity.

Another important extension may be to address the shapes of such vesicles. This issue was already considered for pressurized vesicles. In the case of the 2D Gaussian model, the asphericity was calculated directly as well as measured by simulations [75, 85, 86], revealing anisotropic shapes below the phase transition and circular ones above it. In the three-dimensional case of fluid surfaces the asphericity was measured by Monte Carlo simulations as a function of p [77]. For particle-encapsulating vesicles, we do not suspect a conceptually different behavior. Nevertheless, this issue is yet to be addressed.

# Appendices

## Appendix A: 2D Freely Jointed Chain under Tension

In this Appendix we recall the results for the partition function of a 2D, *open*, freely jointed chain subject to a tensile force. These results are used in Sections 3.2.2 and 3.2.4.

Consider a 2D freely jointed chain composed of N links of length  $l \equiv 1$ . A chain configuration is defined by N 2D unit vectors,  $\{\mathbf{u}_j\}_{j=1,\dots,N}$ , specifying the orientations of the links. One end of the chain is held fixed while the other is pulled by a force **f** (measured in units of  $k_{\rm B}T/l$ ). The partition function of the chain is

$$Z(\mathbf{f},N) = \int \prod_{j=1}^{N} d\mathbf{u}_j e^{\mathbf{f} \cdot \mathbf{u}_j} = \left(\int_0^{2\pi} d\theta e^{f\cos\theta}\right)^N = [2\pi I_0(f)]^N.$$
(A.1)

The mean end-to-end vector is obtained from Eq. (A.1) as

$$\mathbf{R} = \nabla_{\mathbf{f}} \ln Z = N \frac{I_1(f)}{I_0(f)} \mathbf{\hat{f}}.$$
(A.2)

The mean end-to-end distance in the limit of weak force, to two leading orders, is

$$R/N \simeq f/2 - f^3/16,$$
 (A.3)

leading, upon inversion, to

$$f \simeq 2R/N + (R/N)^3.$$
 (A.4)

Finally, the free energy for fixed end-to-end distance (to two leading orders in small R/N) is

$$F(R) = -\ln Z[\mathbf{f}(\mathbf{R})] + \mathbf{f} \cdot \mathbf{R} \simeq \frac{R^2}{N} + \frac{R^4}{4N^3}.$$
 (A.5)

This yields the usual Gaussian term,  $F_{\rm el}$ , and the first correction due to inextensibility,

 $F_{\text{inext}}$ , used in Eq. (3.4).

## Appendix B: Area Probability Distribution Function of Highly Swollen Freely Jointed Rings

Unlike the probability distribution function of the area for a Gaussian ring,  $P_0^{\rm G}(N, V)$  of Eq. (3.41), its counterpart for a freely jointed ring,  $P_0^{\rm FJ}(N, V)$ , is not known analytically. The asymptote of  $P_0^{\rm FJ}$  as  $V \to V_{\rm max}$ , nonetheless, can be calculated, which is the aim of this Appendix.

A configuration of the ring is defined by a set of N 2D vectors specifying the monomer positions,  $\{\mathbf{r}_j\}_{j=0,\dots,N}$  with  $\mathbf{r}_0 = \mathbf{r}_N$  to make the chain closed. The partition function for a fixed area V is given by

$$Z^{\mathrm{FJ}}(N,V) = \int \prod_{j=1}^{N} d\mathbf{r}_{j} \delta(|\mathbf{r}_{j} - \mathbf{r}_{j-1}| - 1) \delta(V'[\{\mathbf{r}_{j}\}] - V)$$

$$= \int dp \int \prod_{j=1}^{N} d\mathbf{r}_{j} e^{ip(V'[\{\mathbf{r}_{j}\}] - V)} \delta(|\mathbf{r}_{j} - \mathbf{r}_{j-1}| - 1),$$
(B.1)

where  $V'[\{\mathbf{r}_j\}]$  is the area of the configuration  $\{\mathbf{r}_j\}$ .

When the ring statistics is governed by highly swollen configurations, the integration over  $\{\mathbf{r}_j\}$  can be performed analytically using the transfer-matrix technique (see Section 3.2.4). This leads to

$$Z^{\rm FJ}(N,V \lesssim V_{\rm max}) = \int dp e^{-ipA} \left[ 2\pi I_0 \left( \frac{ipN}{4\pi} \right) \right]^N, \qquad (B.2)$$

where  $I_0$  is the zeroth-order modified Bessel function of the first kind. The asymptotic expansion of  $I_0$  for large arguments,

$$I_0\left(\frac{ipN}{4\pi}\right) \simeq \left(\frac{2}{ipN}\right)^{1/2} e^{\frac{ipN}{4\pi}},\tag{B.3}$$

is substituted in Eq. (B.2). This yields, up to a constant prefactor,

$$Z^{\rm FJ}(N,V \lesssim V_{\rm max}) \sim \int dp e^{ip(V_{\rm max}-V)} (pN)^{-N/2}, \qquad (B.4)$$

which, upon a simple change of variables (or, alternatively, a stationary-phase approximation) leads to

$$Z^{\rm FJ}(N,V \lesssim V_{\rm max}) \sim (V_{\rm max} - V)^{N/2}.$$
 (B.5)

Thus, the area probability distribution function, which is proportional to  $Z^{\text{FJ}}$ , is

given to leading order in  $(V_{\text{max}} - V)$  by

$$P_0^{\rm FJ}(N, V \lesssim V_{\rm max}) \sim (V_{\rm max} - V)^{N/2}.$$
 (B.6)

This result is used in Section 3.3.3 to calculate the mean area of a freely jointed ring in the strong-swelling regime. In Chapter 6 we show that this expression is an example of a more general result for highly swollen envelopes.

## Appendix C: Microscopic Model of Nearly Spherical Vesicles

In Chapter 6 we present a general thermodynamic treatment of any closed particleencapsulating compartment regardless of its microscopic description. The results, of course, should be valid for any specific model. Here we consider a specific case of nearly spherical vesicles with a fixed surface area A and, thus, a maximum volume. We will first derive the volume probability distribution function and then the correlation function of shape fluctuations.

The shape of such swollen objects can be parameterized by the distance of the envelope from its center of mass as a function of solid angle,  $R(\theta, \varphi)$ . This radial coordinate can be expanded around that of a sphere,  $R_A$ , as a series of spherical harmonics,

$$R(\theta,\varphi) = R_A \left[ 1 + \sum_{l\geq 0}^{l_{\max}} \sum_{m=-l}^{l} u_{lm} Y_{lm}(\theta,\varphi) \right], \qquad (C.1)$$

where  $R_A = \sqrt{A/(4\pi)}$  and  $u_{lm} = (-1)^m u_{lm}^*$ . The total number of degrees of freedom is  $N + 4 \equiv l_{\max}(l_{\max} + 2) \sim A$ . In such a representation the volume is given, to second order in  $u_{lm}$ , by

$$V(\{u_{lm}\}) = R_A^3 \left\{ \frac{4\pi}{3} \left[ 1 + \frac{u_{00}}{\sqrt{4\pi}} \right]^3 + \sum_{l \ge 1}^{l_{\max}} \sum_{m=-l}^{l} |u_{lm}|^2 \right\},$$
(C.2)

and the area by

$$A(\{u_{lm}\}) = R_A^2 \left\{ 4\pi \left[ 1 + \frac{u_{00}}{\sqrt{4\pi}} \right]^2 + \sum_{l \ge 1}^{l_{\max}} \sum_{m=-l}^{l} |u_{lm}|^2 [1 + l(l+1)/2] \right\}.$$
 (C.3)

Applying the constraint of fixed area,  $A(\{u_{lm}\}) = A$ , is equivalent, up to  $O(u_{lm}^2)$ , to fixing

$$u_{00} = -\left\{\sum_{l\geq 1}^{l_{\max}} \sum_{m=-l}^{l} |u_{lm}|^2 [1+l(l+1)/2]\right\} /\sqrt{16\pi}.$$
 (C.4)

Substituting Eq. (C.4) in Eq. (C.2) yields, up to  $O(u_{lm}^2)$ ,

$$V(\{u_{lm}\}) = V_{\max} - \frac{R_A^3}{4} \left[ \sum_{l\geq 1}^{l_{\max}} \sum_{m=-l}^{l} |u_{lm}|^2 (l+2)(l-1) \right] \equiv V_{\max} - \sum_{l,m} |u_{lm}|^2 W_l, \quad (C.5)$$

where  $V_{\rm max} = 4\pi R_A^3/3$  is the maximum volume of the vesicle, and we define  $W_l \equiv$ 

 $3(l+2)(l-1)V_{\text{max}}/(16\pi)$ . The harmonics with l = 1 represent pure translations [132] and are thus omitted. From here onwards summation over l and m implies summing over l > 1 and  $-l \le m \le l$ , *i.e.*, a total of N modes.

We now calculate the probability distribution function of volumes for this model,

$$P_{A}(V) = \int \mathcal{D}u_{lm}\delta(V - V[\{u_{lm}\}]) = \int \mathcal{D}u_{lm}\int \frac{dp}{\sqrt{2\pi}}e^{ip(V - V[\{u_{lm}\}])}$$
  
$$= \int \frac{dp}{\sqrt{2\pi}}e^{ip(V_{\max}-V)}\int \mathcal{D}u_{lm}e^{-ip\sum_{l,m}|u_{lm}|^{2}W_{l}}$$
  
$$= \prod_{l,m} \left[\frac{\pi}{W_{l}}\right]^{1/2}\frac{K^{N}}{\sqrt{2\pi}}\int dp\frac{e^{ip(V_{\max}-V)}}{(ip)^{N/2}}$$
  
$$= \prod_{l,m} \left[\frac{4\pi}{R_{A}^{3}(l+2)(l-1)}\right]^{1/2}\frac{K^{N}}{\sqrt{2\pi}}(V_{\max}-V)^{N/2-1}\int \frac{dxe^{ix}}{(ix)^{N/2}}$$
  
$$\sim (V_{\max}-V)^{N/2-1},$$
  
(C.6)

where  $K \equiv \int dx e^{-ix^2}$ . This result is similar to the one obtained for a highly swollen freely jointed ring in Appendix B, Eq. (B.6).

For vesicles such as those studied in Chapter 6, *i.e.*, encapsulating an ideal solute and subject to an external pressure difference  $p_{o}$ , the partition function is given by

$$Z(Q, p_{\rm o}, N) = \int \mathcal{D}u_{lm} e^{-p_{\rm o}V(\{u_{lm}\}) + Q\log V(\{u_{lm}\})},$$
(C.7)

where Q is the number of trapped particles. This may also be written as

$$Z(Q, p_{o}, N) = \int dV \int \mathcal{D}u_{lm} e^{-p_{o}V(\{u_{lm}\}) + Q \log V(\{u_{lm}\})} \delta(V - V[\{u_{lm}\}])$$
  
=  $\int dV e^{-p_{o}V + Q \log V} \int \frac{dp}{\sqrt{2\pi}} e^{-ip(V_{\max} - V)} \int \mathcal{D}u_{lm} e^{ip\sum_{l,m} |u_{lm}|^{2}W_{l}},$  (C.8)

where we have used Eq. (C.5). Calculating this integral, in a procedure similar to that described in Eq. (C.6), leads to the following partition function:

$$Z(Q, p_{\rm o}, N) = \prod_{l,m} \left[ \frac{\pi K^2}{W_l} \right]^{1/2} \frac{1}{\sqrt{2\pi}} \left( \int \frac{dx e^{ix}}{(ix)^{N/2}} \right) \int dV (V_{\rm max} - V)^{N/2 - 1} e^{-p_{\rm o}V + Q \log V}.$$
(C.9)

This expression is substituted for  $Z_v$  in Eq. (6.1).

We proceed to calculate the shape correlation function  $\langle u_{lm}u_{l'm'}\rangle$ . This is done by

adding a dummy variable  $\lambda_{lm}$ ,

$$Z(Q, p_{o}, N) = \int dV e^{-p_{o}V + Q \log V} \int \frac{dp}{\sqrt{2\pi}} e^{ip(V_{\max} - V)} \int \mathcal{D}u_{lm} e^{-ip\sum_{l,m} |u_{lm}|^{2}W_{l} + \sum \lambda_{lm}u_{lm}} \Big|_{\lambda_{lm} = 0}$$
  
$$= \prod_{l,m} \left[ \frac{\pi K^{2}}{W_{l}} \right]^{1/2} \int dV e^{-p_{o}V + Q \log V} \int dp \frac{e^{ip(V_{\max} - V) + i\sum \lambda_{lm}^{2}/(4pW_{l})}}{\sqrt{2\pi}(ip)^{N/2}} \Big|_{\lambda_{lm} = 0}.$$
  
(C.10)

To obtain the correlation function one needs to differentiate Z with respect to  $\lambda_{lm}$ (prior to the substitution of  $\lambda_{lm} = 0$ ),

$$Z\langle u_{lm}u_{l'm'}\rangle = \frac{\partial^2 Z}{\partial\lambda_{lm}\partial\lambda_{l'm'}} = \delta_{ll'}\delta_{m,-m'}\prod_{l,m}\frac{1}{\sqrt{2\pi}} \left[\frac{\pi K^2}{W_l}\right]^{1/2} \int dV e^{-p_o V + Q\log V} \frac{-2}{4W_l} \int dp \frac{e^{ip(V_{\max}-V)}}{(ip)^{N/2+1}} = \prod_{l,m} \left[\frac{\pi K^2}{W_l}\right]^{1/2} \frac{-1}{2W_l\sqrt{2\pi}} \left(\int \frac{dxe^{ix}}{(ix)^{N/2+1}}\right) \int dV e^{-p_o V + Q\log V} (V_{\max}-V)^{N/2}.$$
(C.11)

This may be written as

$$\langle u_{lm}u_{l,-m}\rangle = \frac{-1}{2W_l} \langle V_{\max} - V\rangle \left( \int \frac{dxe^{ix}}{(ix)^{N/2+1}} \right) / \left( \int \frac{dxe^{ix}}{(ix)^{N/2}} \right)$$

$$= \frac{16\pi}{3N(l+2)(l-1)} \frac{V_{\max} - \langle V\rangle}{V_{\max}}, \quad l > 1.$$
(C.12)

Equation (C.12) decribes how fluctuations are supressed as  $\langle V \rangle$  approaches  $V_{\text{max}}$ .

Let us compare this result with the one for a flat membrane under surface tension  $\sigma$  and no bending rigodity. In this case the mean square height fluctuation is given by

$$\langle h_{\mathbf{q}}^2 \rangle = \frac{1}{L^2 \sigma q^2},\tag{C.13}$$

where **q** is the wavevector, and L is the lateral dimension of the membrane. The spherical representation coincides with the flat one in the limit  $R_A \to \infty$  and  $l \to \infty$ such that  $q^2 = l(l+1)/R_A^2$  is finite and  $L^2 = 4\pi R_A^2$ . Comparison of Eqs. (C.12) and (C.13) reveals that they are equivalent once we identify the surface tension as

$$\sigma \sim \frac{R_A N}{V_{\text{max}}} \frac{V_{\text{max}}}{V_{\text{max}} - \langle V \rangle}.$$
 (C.14)

This result for the surface tension coincides with the one obtained more generally in

Chapter 6, Eq. (6.13).

### Appendix D: Microscopic Model of Nearly Circular Rings

Here we present another microscopic description of the more general system discussed in Chapter 6 — that of nearly circular two-dimensional rings. The mathematical treatment is almost identical to the more complex three-dimensional system discussed in the preceding appendix.

We consider a ring with a given perimeter A. Its contour is defined by the distance R from the ring's center of mass as a function of the polar angle  $\varphi$ . For swollen rings,  $R(\varphi)$  is expanded around the radius of a circle  $R_A$  as a series of N eigenmodes,

$$R(\varphi) = R_A \left( 1 + \sum_{m=-N/2}^{N/2} u_m e^{im\varphi} \right), \qquad (D.1)$$

where  $R_A \equiv \sqrt{A/(2\pi)}$  and  $u_m = (-1)^m u_{-m}$ .

In this representation the area (two-dimensional volume) and perimeter are given to second order in  $u_m$  by

$$V(\{u_m\}) \simeq \pi R_A^2 \left[ (1+u_0)^2 + \sum_{m \neq 0} u_m^2 \right],$$
 (D.2)

$$A(\{u_m\}) \simeq 2\pi R_A(1+u_0) + \pi R_A \sum_{m \neq 0} m^2 u_m^2.$$
 (D.3)

Applying the fixed perimeter constraint  $A(\{u_m\}) = A$  is equivalent, up to  $O(u_m^2)$ , to fixing

$$u_0 = -\frac{1}{2} \sum_{m \neq 0} m^2 u_m^2. \tag{D.4}$$

Substituting Eq. (D.4) in Eq. (D.2) gives, up to  ${\cal O}(u_m^2),$ 

$$V(\{u_m\}) = V_{\max} \left[ 1 + \sum_{m \neq 0} (1 - m^2) u_m^2 \right] \equiv V_{\max} - \sum_{m \neq 0} W_m u_m^2,$$
(D.5)

where  $V_{\rm max} = A^2/(4\pi)$  and we denote

$$W_m \equiv V_{\max}(m^2 - 1). \tag{D.6}$$

Note that the contribution of the  $m = \pm 1$  modes vanish. This result is analogous to Eq. (C.5) of Appendix C and since further calculations in the previous appendix were performed for a general weight function  $W_m$  they hold also for this two-dimensional case.

For example, the distribution function of volumes for a 2D ring is given, according to Eqs. (C.6) and (D.6), by

$$P_{A}(V) = \prod_{|m|>1} \left[\frac{\pi}{W_{m}}\right]^{1/2} \frac{K^{N}}{\sqrt{2\pi}} \int dp \frac{e^{ip(V_{\max}-V)}}{(ip)^{N/2}}$$
$$= \prod_{|m|>1} \left[\frac{\pi}{V_{\max}(m^{2}-1)}\right]^{1/2} \frac{K^{N}}{\sqrt{2\pi}} (V_{\max}-V)^{N/2-1} \int \frac{dxe^{ix}}{(ix)^{N/2}}$$
(D.7)
$$\sim (V_{\max}-V)^{N/2-1},$$

where K was defined already in Appendix C as  $K \equiv \int dx e^{-ix^2}$ . This result was obtained in a different manner in Appendix B, Eq. (B.6).

The partition function of a ring, encapsulating a fixed number Q of ideal particles and subject to an external pressure difference is given, according to Eq. (C.9), by

$$Z(Q, p_{\rm o}, N) = \prod_{|m|>1} \left[\frac{\pi K^2}{W_m}\right]^{1/2} \frac{1}{\sqrt{2\pi}} \left(\int \frac{dx e^{ix}}{(ix)^{N/2}}\right) \int dV (V_{\rm max} - V)^{N/2 - 1} e^{-p_{\rm o}V + Q\log V},$$
(D.8)

and, thus, the correlation function of the shape fluctuations  $\langle u_m u_{-m} \rangle$  is given according to Eqs. (C.12) and (D.6) by

$$\langle u_m u_{-m} \rangle = \frac{1}{N(m^2 - 1)} \frac{V_{\max} - \langle V \rangle}{V_{\max}}, \quad |m| > 1.$$
 (D.9)

Equation (D.9) describes how fluctuations are suppressed as the ring approaches a circular shape.
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