Phases and fluctuations in a model for asymmetric inhomogeneous fluid membranes

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We propose and analyze a model for phase transitions in an inhomogeneous fluid membrane, that couples local composition with curvature non-linearly. For asymmetric membranes, our model shows generic non-Ising behavior and the ensuing phase diagram displays either a first- or a second-order phase transition through a critical point (CP) or a tricritical point (TP), depending upon the bending modulus. It predicts generic nontrivial enhancement in fluctuations of asymmetric membranes that scales with system size in a power law fashion at the CP and TP in two dimensions, not observed in symmetric membranes. It also yields two-dimensional Ising universality class for symmetric membranes, in agreement with experimental results.

I. INTRODUCTION

Recent experiments on giant plasma membrane vesicles (GPMVs) isolated from living cells and model membranes (e.g., artificially prepared lipid bilayers made of lipids and cholesterol) display lateral inhomogeneities over length scales much larger than the typical sizes of the constituent lipid and protein molecules and stay in coexisting liquid-ordered ($L_o$) and liquid-disordered ($L_d$) phases \textsuperscript{1,2,3}. The universal scaling exponents that characterize the miscibility transition in GPMVs or model lipid bilayers are experimentally found to be close to those of the two-dimensional (2D) Ising model \textsuperscript{4,5}. Ref. \textsuperscript{6}, by using lattice-based Monte-Carlo simulations, studies phase separations and critical fluctuations in two-component lipid membranes, and discusses the possibility of both quasi-abrupt transitions (first order transitions) and second order transitions, depending upon the details of lipid compositions. Plasma membranes of living cells are however asymmetric \textsuperscript{7}. This asymmetry may affect the macroscopic properties at the critical point \textsuperscript{8}, although the knowledge about it is still at a preliminary level \textsuperscript{9}. Hence, in the absence of detailed experimental results on the possible universal scaling properties of phase transitions in asymmetric membranes, studies of phase transitions in asymmetric membranes theoretically by using models with definite symmetries should be welcome. In particular, studies on how a generic curvature-composition non-linearity, allowed by specific symmetry considerations, can affect the resulting phase behavior of the model, should be of interest.

In this article we ask whether asymmetry in an inhomogeneous fluid membrane can significantly enhance fluctuations near phase transitions. Since any purported effects of asymmetry are likely to depend on how asymmetry affects the system free energy, we theoretically propose and study a model belonging to a particular symmetry for phase transitions in both symmetric and asymmetric inhomogeneous membranes. Our model is a reduced model, in which the bilayer nature is not kept explicitly; instead it is replaced effectively by an inhomogeneous single layer for simplicity. Our main results are that depending upon the bending modulus $\kappa$ the composition field that describes the inhomogeneity of the asymmetric membrane in our model may display (i) both first and second order phase transition through a critical point (CP) and (ii) a tricritical point (TP). In addition, our model predicts generic nontrivial enhancement of fluctuations of asymmetric inhomogeneous membranes near TP and CP with a variance that depends on the system size $L$ in a power law fashion in two dimensions. Further in our model, it is necessarily of second order belonging to the 2D Ising universality class for symmetric membranes. We provide a mean-field (MF) analysis of the phase diagram of the model and calculate the universal scaling exponents that characterize the CP and TP in our model by using perturbative renormalization group (RG) methods. Unlike more commonly used linear curvature-composition coupling \textsuperscript{10}, our model involves non-linear curvature-composition coupling belonging to a particular symmetry (see below). Thus it should be useful in understanding the general implications of non-linear curvature-composition relationships in experiments on membranes \textsuperscript{11}. Validity of our model and the results that follow may be tested by measuring fluctuations in asymmetric inhomogeneous membranes and used to contrast with symmetric membranes. From perspectives of theoretical physics, our model is an example of a fluid membrane with internal degrees of freedom that displays rich critical behavior. The rest of the article is organized as follows: In Sec. \textsuperscript{II} we construct our model. We then discuss the mean-field analysis of our model in Sec. \textsuperscript{III}, following by enumeration of the scaling exponents in Sec. \textsuperscript{IV}. We conclude and summarize our results in Sec. \textsuperscript{V}.

II. CONSTRUCTION OF THE MODEL

A real asymmetric lipid bilayer generally consists of two lipid monolayers, which are constitutionally different (i.e., non-identical), e.g., cell membranes of eukary-
otic cells [7]. There are microscopic processes (e.g., flip-flop [7]) which lead to exchange of the constituent molecules between the two monolayers of a bilayer. However, these exchange processes are typically very slow. In addition, there are biochemical processes which may favor maintaining compositional differences across the leaflets [12]. Thus, the compositions of the two leaflets over relevant physical and biological time scales may be very different. Coarse-grained models for an asymmetric lipid bilayer thus require two sets of scalar fields, one for each for the monolayers, representing the compositional degree of freedom in the corresponding monolayer, see, e.g., Refs. [13] for details. We, however, use a simpler approach, where a single field $\phi$ is used together with a height field to mathematically describe an asymmetric membrane. Here, the asymmetry is no longer described by the composition differences between the two monolayers, but rather by the breakdown of the inversion symmetry of the membrane. Thus, effectively, only a single layer is considered instead of a bilayer structure. There is already a substantial body of work that uses a single composition field degree of freedom, together with a height field, to model an asymmetric inhomogeneous membrane; see, e.g., Refs. [10]. Our model is in the same spirit as them.

Here are the details of our model: We use a coarse-grained description to build our model. For simplicity, we ignore the bilayer structure, and model it implicitly by a single inhomogeneous fluid membrane, microscopically made up of two components (say, two types of lipids), $A$ and $B$, with local concentrations $n_A$ and $n_B$, with vanishing surface tension [13], described by a height field $h(x, y)$ in the Monge gauge [12] and the concentration difference field $\phi \equiv [n_A(x) - n_B(x)]$, as the relevant compositional degree of freedom, since we are interested in phase transitions in the membrane [13], and $x = (x, y)$. The detailed form of the free energy functional depends sensitively on the underlying symmetry of the model system. We choose $\phi$ to have the Ising-symmetry, interacting via local ferromagnetic Ising-like interactions [3]. Further, the system being asymmetric is not invariant under the inversion symmetry $h \rightarrow -h$. Our imposition of these symmetries for an asymmetric membrane, dictates that the system and hence the corresponding free energy functional $F$ should be invariant under $(\phi, h) \rightarrow (-\phi, -h)$ (hereafter SYMII). Thus, in our model, one may have symmetry-allowed curvature-composition coupling of the form $\lambda \phi^2 \nabla^2 h + \lambda_1 \phi^2 (\nabla^2 h)^2$. In contrast, symmetric membrane models are typically invariant separately under $\phi \rightarrow -\phi$ and $h \rightarrow -h$ (SYMIII). Therefore, taking everything into consideration $F$ is

$$F = \int d^2 x \left[ \frac{r}{2} \phi^2 + \frac{b}{2} (\nabla \phi)^2 + \frac{u}{4!} \phi^4 + \frac{v}{6!} \phi^6 \right] + \frac{\kappa}{2} (\nabla^2 h)^2 + \lambda \phi^2 \nabla^2 h + \lambda_1 \phi^2 (\nabla^2 h)^2,$$

where $r \sim (T - T_c)$ with $T_c$ as the MF critical temperature for $\phi$, and taking $\phi$ (having the dimension of concentration) to scale as $1/\xi^2$, $b \sim K_B T \xi^2$ (in 2D) is a measure of energy-scale associated with composition fluctuations, where $K_B$ is the Boltzmann constant and $\xi_0$ is (microscopic) correlation length of the order of a few angstroms. Coupling constants $u > 0$ and $v > 0$ determine the strengths of lipid-lipid interactions; $u_0^2$-term is added for thermodynamic stability (see below). The $\lambda$ term is related to a local spontaneous curvature $c_0(\phi) = -\lambda \phi^2 / \kappa$ [17, 18]. Alternatively, it may be viewed as a local fluctuation in $T_c$, such that local critical temperature $T_{c-L} = T_c - 2 \lambda \nabla^2 h$. Coupling constant $\lambda$ embodies asymmetry in the model and implicitly contains information about geometry (e.g., shape, packing) and asymmetric distribution of lipid molecules in the system. On physical grounds, following the arguments in Ref. [10], we set $\lambda \xi_0^2 \sim \kappa H_0$, where $n_0 \sim 1/\xi_0^2$ is a mean concentration and $H_0 \sim 10^6 m^{-1}$ is a typical (molecular) spontaneous curvature. This yields $\lambda \sim \kappa H_0 \xi_0^2$. Since $\xi_0$, the microscopic correlation length, should scale with the linear size of the constituent lipid molecules, $\lambda$ may be experimentally varied by considering samples made of lipids of different molecular sizes. Of course, for a pure fluid membrane $\phi = 0$ [19]. Notice that our model is not the most generic in that a SYM II violating asymmetric linear curvature-composition coupling term may be present. Effects of such a coupling, i.e., $c_0(\phi)$ being proportional to $\phi$ with the system invariant under $(\phi, h) \rightarrow (-\phi, -h)$ (hereafter SYMIII), have been extensively studied [10]. Our choice of curvature-composition coupling is made for the purpose of illustration [20] and complementary to that in Refs. [10]. Furthermore, the $\lambda_1$-term may be interpreted as a contribution to $T_{c-L}$ or to a local (effective) bending modulus $\kappa_2 = \kappa + 2 \lambda_1 \phi^2$. Here, we have omitted the geometric nonlinearities, which are subdominant to the existing nonlinear terms (the $u$- and $\lambda$-terms) [15, 21, 22]. Note that the absolute sign of $\lambda$ is arbitrary and may be switched by $h \rightarrow -h$. The $\lambda$-term violates the inversion symmetry $h \rightarrow -h$; where as for a symmetric membrane one has $\lambda = 0$, leading to invariance under SYMII. Lastly, since our model effectively assumes the bilayer to be a single incompressible sheet, it is unable to capture the effects of coupling of the local bending and densities of the two monolayers [23], which yields a new slow mode related to fluctuations in the density difference in the two monolayers. Notice that in constructing our model we have been guided solely by general symmetry considerations, without any reference to microscopic or molecular level details. We believe it is useful to theoretically construct models with specific symmetry using this approach and study the ensuing macroscopic consequences, in view of the relative lack of quantitative results on the universal scaling properties of phase transitions in asymmetric membranes, in comparison with their symmetric counterparts.
III. MEAN-FIELD ANALYSIS

It is instructive to begin with a MF analysis for the phase transitions in the model, ignoring the \( \lambda_1 \)-term (it is subdominant to the existing terms; see below). The MF is constructed by ignoring all spatial correlations and in terms of constant values of the order parameter field \( \phi = m \) and the curvature \( \nabla^2 h = c \). Here, \( c \) and \( m \) may both be zero or non-zero depending upon the phase concerned. The geometric nonlinearities are neglected. First consider a symmetric membrane, for which within MF, \( c = \nabla^2 h = 0 \) for all \( T \) and \( \phi = m = 0 \) for \( T \geq T_c \), and \( \phi = m \neq 0 \) for \( T < T_c \), respectively, thus yielding Ising-like MF behavior with a second-order transition at \( T_c \). In contrast, for an asymmetric membrane at the MF level for \( T \geq T_c \) one obtains, \( c = \kappa \nabla^2 h = -\lambda \phi^2 = -\lambda m^2 = 0 \). However, for \( T < T_c \), one has \( \phi = m \neq 0 \), thus giving \( c = -\lambda m^2 \), implying a non-zero radius of curvature for an asymmetric membrane in the ordered phase. Ignoring the spatial correlations of \( \phi \) in the spirit of MF analyses, an effective Landau free energy \( \mathcal{F}_e \) for a constant \( \phi = m \) may now be constructed by replacing \( c \). It has the form

\[
\mathcal{F}_e = \frac{r}{2} m^2 + \tilde{u} \eta m^4 + \eta m^6 ,
\]

where \( \tilde{u} \equiv u - a \lambda^2 / \kappa \) (\( a > 0 \) is a \( O(1) \) numerical coefficient) can be \( \tilde{u} \) positive, negative or zero. Within the mean field picture, the effective Landau free energy \( \mathcal{F}_e \) may be analysed in a standard way \([25]\): one finds the following possibilities: (i) A CP at \( r = 0 \) with \( \tilde{u} > 0 \), (ii) a first order phase transition at \( r = |\tilde{u}|^2/(2\nu) = |u - a \lambda^2 / \kappa|^2/(2\nu) \) for \( \tilde{u} < 0 \), and (iii) a TP at \( r = 0 \), \( \tilde{u} = 0 \), i.e., \( u = a \lambda^2 / \kappa \) as schematically shown in Fig. 1 this phase diagram is identical to that observed in the normal-superfluid transition in liquid helium mixtures \([24]\). Evidently, from its definition as given above \( \tilde{u} > 0 \) or \( < 0 \) for large or small \( \kappa \), respectively, implying lipid domain formations proceed through second or first order transitions for stiff (large \( \kappa \)) or soft (small \( \kappa \)) membranes, respectively. We now critical exponents \( \eta_\phi \) and \( \nu \) through the relations \( \langle \phi(x) \phi(0) \rangle \sim |x|^{2-\phi \eta_\phi} \) for fixed \( |x|/\xi_\phi \) where \( \xi_\phi \sim |T - T_c|^{-\nu} \) is the correlation length. Thus, one finds from the MF theory \([26]\) \( \eta_\phi = 0 \) and \( \nu = 1/2 \) at both CP and TP. The presence of the first order transition in this model clearly underlines the requirement of a \( \nu \phi^8 \) term in \( F \) for thermodynamic stability.

We shall see below that \( \kappa_e \) becomes scale-dependent, i.e., it depends on the local scale \( \ell \). Since \( \langle \phi(q) \phi(-q) \rangle \) is positive definite, \( \kappa_e < \kappa \) generally, opening up the possibility of \( \kappa_e \) being zero or negative. Since \( \kappa_e \) is generically smaller than \( \kappa \), the asymmetric membrane will be generically softer or more flexible than a pure fluid membrane, a feature that should also be displayed by models belonging to SYMIII \([10]\), which use bilinear curvature-composition coupling. One may further define a persistence length \( \xi_p \), such that \( \kappa_e(l = \xi_p) = 0 \). Noticing that for a system with linear size \( L \), the correction to \( \kappa_e \) scales as \( L^2 \) in 2D at the MF level; given by \( r = 0 \), we find \( \xi_p \sim |\kappa/(\lambda^2)|^{1/2} \), thus \( \xi_p \sim 1/\lambda \) for fixed \( \kappa \) and \( T \). Physically, this essentially gives a linear scale over which the membrane remains flat. Clearly, in our model, for an experimentally accessible asymmetric membrane with nearly flat conformation, (bare) \( \lambda \) should be sufficiently small, such that \( \xi_p \gg L \), linear dimension of the system. However, for quantitative predictions on \( \xi_p \), one requires to have a numerical estimate of \( \ell \), which at present is lacking. Construction of atomistic models and numerical studies on them linking microscopic structures with macroscopic properties or parameters (e.g., \( \kappa, \lambda \)) would be useful \([27]\), which are beyond the scope of this work. For \( \kappa_e < 0 \), our model shows instabilities akin to Refs. \([10]\). Notice however that the instabilities here for \( \kappa_e < 0 \) are due to a nonlinear curvature-composition coupling, unlike for models in Refs. \([10]\), where bilinear curvature-composition couplings are responsible for the instabilities. In the remaining part of the article below, we only consider \( \kappa_e > 0 \). Furthermore, considering that \( \kappa_e \) has got a \( O(L^2) \) (perturbative) correction to its bare value \( \kappa \) coming from the curvature-composition interaction, thence at 2D, with \( n = \nabla h \) as the local normal to the membrane (to the leading order in smallness), the variance of \( n \) has a (perturbatively obtained, ignoring logarithms) contribution

\[
\Delta = \langle n^2(x) \rangle \sim O(\lambda^2 L^2) ,
\]

in addition to the contribution from (bare) \( \kappa \). Thus, \( \Delta \) formally diverges as \( L \to \infty \). This is significantly stronger than the well-known \( \log L \) dependence of \( \Delta_s = \langle n^2(x) \rangle \) that ensues for a pure symmetric fluid membranes \([13]\). Even for an inhomogeneous symmetric membrane, \( \Delta_s \) must have a weaker \( L \)-dependence than \( L^2 \), since the dominant nonlinearity responsible for the \( L^2 \) behavior (i.e., the \( \lambda \)-term) in our model is always absent for a symmetric membrane. This is thus a feature of an asymmetric membrane described by our model that may be directly testable in experiments and can be contrasted with the same from symmetric membranes.

One may also present an equivalent phase diagram in the \( r - \lambda \) plane: see Fig. 2 for a schematic phase diagram in the \( r - \lambda \) plane.

Compare now with linear curvature-composition models \([10]\) having a curvature-composition coupling of the form \( \lambda \phi \nabla^2 h \) (with \( \lambda = 0 \)). It can be shown in that (a) \( \lambda \) does not contribute to the fluctuation corrections
of \( \phi \); with \( u \) remaining as the most relevant nonlinearity, large-scale properties of \( \phi \) is identical to that of the Ising model, and (b) due to the absence of any nonlinear term there are no non-trivial fluctuation corrections to \( \kappa \) from \( \lambda \), and hence, as long as \( k_c > 0 \), \( h \) is identical to that of a pure fluid membrane. In contrast, our model for asymmetric membranes displays generic non-Ising behavior of \( \phi \) including a first order transition and scale-dependent diverging fluctuations of \( h \). Furthermore, as already pointed out above, for a symmetric membrane with SYMIII at 2D, \( \langle n^2(x) \rangle \sim \log L \) [13], much weaker than its \( L^2 \)-dependence for an asymmetric membrane in our model [28]. We confirm below the existence of CP and TP, extract the corresponding universal scaling exponents and show the divergence of the variance of asymmetric membrane fluctuations in a perturbative RG calculation [29].

IV. SCALING EXPONENTS NEAR CP AND TP

For a symmetric membrane (\( \lambda = 0 \)) the remaining geometric non-linearities are irrelevant at 2D in the presence of the \( u \)-term with upper critical dimension \( d_c = 4 \), and hence are ignored. Effectively, thus in our model there are no relevant coupling between \( \phi \) and \( h \) in a symmetric membrane. Consequently the critical behavior of \( \phi \) is identical to the Ising model, thus belonging to the 2D Ising universality class, already studied extensively in a RG framework [20, 31]: One obtains \( \eta_\phi = c^2/54, \nu_\phi = 1/(2 - \epsilon) \) with \( \epsilon = 4 - d > 0 \) (the \( \phi^6 \) interaction is irrelevant in a RG sense). This is in agreement with experimental results on lipid bilayers by several groups [3, 5]. Further, fluctuation statistics of \( h \) is identical to that of a pure fluid membrane. Assuming a nearly flat conformation (see discussions in the concluding section), predictions from our model is more complicated for an asymmetric membrane for which \( \lambda \neq 0 \) with \( d_c = 4 \), along with \( u \) are relevant couplings (in a RG sense). Thus the ensuing universal scaling behavior at the physically relevant dimension \( d = 2 < d_c \) is expected to be different from both the mean-field scaling behavior for an asymmetric membrane discussed before and 2D Ising behavior of a symmetric membrane. In order to analyze this, we perform a systematic RG analysis of the model following standard procedure well-documented in the literature [30, 31]. In particular, the renormalization Z-factors for the different vertex functions, which are introduced to absorb ultra-violet (UV) divergences in the theory, are calculated by using a dimensional regularization together with a minimal subtraction scheme in terms of an arbitrary momentum scale \( \mu \) [30, 31]. The vertex functions in the present model, which have primitive divergences and hence require renormalization, are given by (the right hand sides of the expressions below are the bare values of the vertex functions in our model that can be easily read off from the free energy functional [11]).

\[
\frac{\delta^2 \Gamma}{\delta \phi_k \delta \phi_{-k}} = r + k^2, \quad (5) \\
\frac{\delta^2 \Gamma}{\delta h_k \delta h_{-k}} = \kappa k^4, \quad (6) \\
\frac{\delta^3 \Gamma}{\delta \phi_q \delta \phi_{-k+q} \delta h_k} = 2\lambda, \quad (7) \\
\frac{\delta^3 \Gamma}{\delta \phi_k \delta \phi_{q_1} \delta \phi_{q_2} \delta \phi_{-k-q_1-q_2}} = u, \quad (8)
\]

where \( \Gamma \) is the vertex generating functional and is the Legendre transform of the free energy corresponding to the partition function [3]: \( k, q, q_1, q_2 \) are Fourier wavevectors. The resulting RG flow equation yields non-trivial scaling of the correlation functions and thermodynamic quantities at the RG fixed points (FP). The relevant Feynman diagrams are shown in the Appendix below.

For calculational convenience we define an implicitly
The FPs are determined by the zeros of the \( \beta \)-functions above: (i) Gaussian (or trivial) fixed point given by \( u_R = 0 = \lambda_R \), (ii) Ising FP given by \( u_R = \epsilon/72, \lambda_R = 0 \), (iii) tricritical FP given by \( u_R = 0, \lambda_R^2 = 0.07\epsilon \) and (iv) nontrivial fixed point (NFP) given by \( u_R = 0.02\epsilon, \lambda_R^2 \approx 0.013\epsilon \). Very small value of \( \lambda_R^2 \) at NFP suggests larger \( \xi_p \) and hence easier experimental accessibility at NFP. Each of these FPs represents a different universality class, characterized by a different set of values of the critical exponents. For example, we find for

- Gaussian FP: \( \eta_\phi = 0 = \eta_h, 1/\nu = 2 \).
- Ising FP: identical to the symmetric membrane case,
- TP: \( \eta_\phi = 0, \eta_h = -0.28\epsilon, \frac{1}{\nu} = 2 + 0.179\epsilon \), and
- NFP: \( \eta_\phi = 0.04\epsilon^2, \eta_h = -0.05\epsilon, \frac{1}{\nu} = 2 - 0.3\epsilon \).

Thus, \( \eta_h < 0 \) at all the FPs, in agreement with our qualitative discussions above on \( \kappa_e < \kappa \). From the scaling exponents calculated above, we find that

- \( C_\phi(|x|) = \langle \phi(x)\phi(0) \rangle \sim |x|^{2-d} \) at the TP,
- \( C_\phi(|x|) \sim |x|^{2-d-d^2/54} \) at the Ising FP,
- \( C_\phi(|x|) \sim |x|^{2-d-0.04\epsilon^2} \) at the NFP,

where \( x \) is a spatial separation vector in \( d \)-dimension. Thus, \( C_\phi(|x|) \) varies most slowly with \( |x| \) at TP. Vanishing \( \eta_\phi \) at this order at TP is fortuitous and does not imply MF result; \( \nu \) picks up correction over its MF value already at this order. Let us find out how the correlation of local normal \( n \) to the membrane surface behaves. Noting that \( \langle n(x)h(0) \rangle \sim |x|^{4-d-\eta_h} \), we find \( \langle n(x)\cdot n(0) \rangle \) scales as \( \sim |x|^{2-d+0.05\epsilon} \) at the NFP and \( \sim |x|^{2-d+0.28\epsilon} \) at the TP. Hence,

- At TP, \( \Delta \sim L^{0.28\epsilon} \).
- At NFP, \( \Delta \sim L^{0.05\epsilon} \).

Compare this with a symmetric inhomogeneous membrane or a pure fluid membrane. Disregarding the geometric nonlinearities (which are irrelevant in a RG sense in the presence of \( u \) and \( \lambda \)), for a symmetric membrane variance \( \Delta_s = \langle n^2(x) \rangle \) varies as \( n\log L \) \( [28] \). Thus, \( \Delta \) depends on \( L \) much more strongly than \( \Delta_s \). For example, measuring lengths in the unit of molecular cut-off \( \sim 10\text{nm} \) and taking \( L \sim 10\mu m \) (typical size of an eukaryotic cell), we find \( \Delta/\Delta_s \sim 10 \) at TP and 2 at NFP. Finally, we consider linear stability of the different FPs. We find \( i \) the Gaussian FP \( u_R = 0, \lambda_R = 0 \) is unstable along both \( u_R \) and \( \lambda_R \) directions, \( ii \) the Ising FP is unstable along the \( \lambda_R \) direction, but stable along the \( u_R \) direction, \( iii \) the TP is unstable along the \( u_R \) direction but stable along the \( \lambda_R \) direction, and finally \( iv \) the NFP is stable along both the directions. Not surprisingly, the TP can be reached only by proper tuning of the parameters. The RG flow lines are schematically described in Fig. 3.

![Fig. 3: A schematic stability diagram of FPs in the \( \lambda_R - u_R \) plane. Arrows indicate stable directions (see text).](image-url)
$h$ and belongs to the 2D Ising universality class, a feature observed in experiments on lipid bilayers and GPMVs [3, 4]. Our results for miscibility transitions in asymmetric inhomogeneous membranes are much more dramatic displaying generic non-2D Ising-like behavior, with both second and first order transitions and a TP. Further, asymmetric membranes are found to have dramatically enhanced $L$-dependent (formally diverging in the thermodynamic limit) fluctuations at TP and CP in 2D, in contrast to symmetric membranes. Thus measurements of membranes fluctuations near CP or TP are important, and should yield signatures of asymmetry and composition-curvature coupling. First order transitions in our model is noteworthy, since a similar possibility has been discussed in Ref. [4, 11]. Experiments on carefully prepared asymmetric membranes (see, e.g., Ref. [33]) by standard, e.g., fluorescence, methods (see, e.g., Ref. [3]) should be useful, although more complicated curvature-composition coupling [11] may be needed for quantitative reproduction of experimental data. At a technical level, for a generic nonlinear coupling of the form $f(\phi)\nabla^2 h$, where $f$ is an arbitrary function of $\phi$, there is a general possibility of nontrivial renormalization of $\kappa$ via nonlinear contributions to the self-energy $\Sigma_{\phi h}$ [30] at various orders of the underlying perturbation expansion. Our results here is a specific example of such a possibility. As mentioned above, asymmetric inhomogeneous membrane models belonging to SYMIII also display reduction in $\kappa_c$ due to composition fluctuations and thus are qualitatively similar to our results. In fact, far away from $T_c$, models belonging to both SYMII and SYMIII yield qualitatively similar behavior for membrane fluctuations (they should, however, predict different phase diagrams for $\phi$). But their predictions for membrane fluctuations differ significantly as $T \rightarrow T_c$ (i.e., near the critical zone), since (considering $\kappa_c > 0$), in the absence of any nonlinear term that involves $h$ in models belonging to SYMIII, there are no nontrivial (scale-dependent) fluctuation corrections to $\kappa$. Hence, a linear curvature composition coupling model cannot lead to any change in the scaling of the asymmetric membrane fluctuations (although the magnitude can be enhanced). In contrast, due to the non-trivial renormalization of $\kappa_c$, asymmetric membrane fluctuations in our model displays enhanced fluctuations near $T_c$, with non-trivial corrections to the scale dependences of the fluctuations. In a recent study on symmetric membranes by Ayton et al [34], the curvature composition coupling is of the form $\phi(\nabla^2 h)^2$, which breaks the Ising symmetry. It can be shown, by integrating the composition field, that $\kappa_c < \kappa$ in the model of Ref. [34], in the model leading to enhancement of membrane fluctuations, qualitatively similar to our results here. Thus, our study may be viewed as an asymmetric membrane analog of Ref. [34], where the Ising symmetry is kept, but the inversion symmetry is broken.

Direct comparisons of our results with experiments on inhomogeneous asymmetric bilayer is difficult, mainly due to the reduced nature of our model. Nonetheless, whether or not mechanisms as discussed in our model is operative in a specific experimental set up, e.g., our predictions on the connection of $\kappa$ with the order of transitions and large fluctuations of asymmetric membranes near TP or CP, may be tested by measuring membrane fluctuations. Complementing our coarse-grained modeling by numerical studies on microscopic models linking microscopic structures with macroscopic properties (e.g., $\kappa, \lambda$) would be useful in the present context [27]. Since the signature and magnitude of the effective coupling $\bar{u}$ depends directly on $\lambda^2/\kappa$, our system may be tuned by controlling the membrane bending stiffness $\kappa$. Alternatively, as discussed earlier, since $\lambda \sim H_0\xi_0^3 \sim \xi_0^3$ (taking $H_0 \sim \xi_0^{-1}$, although $H_0^{-1} > \xi_0$ generally), $\lambda$ can be tuned by considering lipid membranes with lipid molecules having different linear sizes, and hence with different $\xi_0$. Considering the strong dependence of $\lambda$ on $\xi_0$, this should be a promising route. Asymmetric membranes may be prepared and their phase behavior investigated by combining the Langmuir-Blodgett/Schaefer method [35] with fluorescence-based imaging. Membrane fluctuation measurements may be done by spectroscopic methods [36]. Bending modulus $\kappa$ may be tuned experimentally, e.g., by cholesterol or BAR proteins [37]. Accessing TP experimentally is expected to be considerably more difficult due to the additional tuning required. Since $\kappa_c < \kappa$ generally, for a sufficiently large membrane a first order transition may take place, depending upon the value of $\kappa$. . Since in-vivo membranes (e.g., red blood cell membranes) tend to have small but finite shear moduli, it will be interesting to theoretically investigate effects of interactions between in-plane displacements and compositional degrees of freedom. Since the divergence of asymmetric membrane fluctuations occurs exactly at CP or TP, it will also be interesting to study the possibility of budding transitions in our model and if the diverging fluctuations are signatures of the budding dynamics, as discussed in Ref. [38]. Lastly, as we mentioned above, a limitation of our model is the lack of bilayer structure in it. This, as elucidated in Ref. [28], may affect the macroscopic behavior. This can be incorporated by generalizing our single compositional field description to two such fields. Both of these fields should be mutually interacting, representing the interactions between the monolayers, in addition to their couplings with $h$, which should be of the form allowed in SYMII. Analyses of this generalized model, although more complicated, can be done in a straight forward way as here. Qualitative features found in our model should be preserved, in addition to possible emergence of new features, e.g., multicritical points and additional slow mode [28] etc. We hope our results will stimulate further theoretical and experimental works along these directions.
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VII. APPENDIX

Here we show all the relevant one- and two-loop Feynmann diagrams for our model. The internal continuous line denote $\langle \phi(q)\phi(-q) \rangle$ correlator. The internal broken line denote $\langle h(qh(-q)) \rangle$ correlator. The external continuous line stands for $\phi$ and the external broken line stands for $h$.

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FIG. 6: Feynmann diagrams for $u$.

FIG. 7: Feynmann diagrams for $\lambda$.

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[21] These geometric nonlinearities originate from (i) expansion of the area element with respect to the Monge gauge base plane for small height fluctuations and (ii) nonlinear corrections to the form of the mean curvature in the Monge gauge.

[22] There may be an additional symmetry-allowed inversion symmetry breaking geometric nonlinearity of the form $\nabla^2 h (\nabla h)^2$, which may arise in an asymmetric membrane from a linear curvature term in $F$: $\int d^2 \nabla^2 h =\int dxdy \sqrt{1 + (\nabla h)^2 \nabla^2 h} \approx \int dxdy (\nabla h)^2 \nabla^2 h$, since $\int dxdy \nabla^2 h$ does not contribute to the free energy, it being a total derivative. While this term may be relevant (same as the $\lambda$ or $u$-terms) we did not consider this term here for simplicity.

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[29] Since in our model the $\phi$-field, being Ising like, has a lower critical dimension $d_L = 1$ and thus displays the standard order-disorder transition at 2D, with a diverging correlation length near $T_c$, formal and rigorous enumeration of the scaling exponents requires the machinery of RG calculations.

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