Active processes make mixed lipid membranes either flat or crumpled

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Abstract

Whether live cell membranes show miscibility phase transitions (MPTs), and if so, how they fluctuate near the transitions remain outstanding unresolved issues in physics and biology alike. Motivated by these questions we construct a generic hydrodynamic theory for lipid membranes that are active, due for instance, to the molecular motors in the surrounding cytoskeleton, or active protein components in the membrane itself. We use this to uncover a direct correspondence between membrane fluctuations and MPTs. Several testable predictions are made: (i) generic active stiffening with orientational long range order (flat membrane) or softening with crumpling of the membrane, controlled by the active tension and (ii) for mixed lipid membranes, capturing the nature of putative MPTs by measuring the membrane conformation fluctuations. Possibilities of both first and second order MPTs in mixed active membranes are argued for. Near second order MPTs, active stiffening (softening) manifests as a super-stiff (super-soft) membrane. Our predictions are testable in a variety of \textit{in vitro} systems, e.g. live cytoskeletal extracts deposited on liposomes and lipid membranes containing active proteins embedded in a passive fluid.

1. Introduction

Cell membranes are generally made of several lipids and have complex structures \cite{1}. The dynamics of cell membranes are affected by biological active (nonequilibrium) processes (e.g. nonequilibrium fluctuations of cell cytoskeletons \cite{2} and active proteins in the lipid membrane \cite{3}); see also \cite{4}. Miscibility phase transitions (MPTs) in equilibrium heterogeneous or mixed model lipid bilayers and giant plasma membrane vesicles (GPMVs) are well studied \cite{5,6}. In contrast, occurrence of MPTs in eukaryotic cell membranes, remains controversial till date \cite{7}. Whether cellular active processes can control membrane fluctuations and associated MPTs in mixed membranes and if so, how, form general motivations for the present study.

Structural and dynamical complexities of cell membranes preclude simple physical understanding of MPTs in cell biological context. This calls for studying this question within a simpler nonequilibrium model appropriate for an \textit{in vitro} setting, where this issue may be addressed systematically and possibly verified in suitably designed \textit{in vitro} experiments. To this end, in this article we construct a hydrodynamic theory for planar active mixed lipid (fluid) membranes \cite{1}. Hydrodynamic approaches have a long history of applications in both equilibrium \cite{8,9} and nonequilibrium \cite{10,11} systems and are successful in predicting general physical properties at large scales independent of the microscopic (molecular) details of the systems. In particular, our theory is applicable to a variety of systems, e.g. a lipid bilayer in an orientable active fluid \cite{10} in its isotropic phase \cite{12} or a lipid bilayer with an active component, e.g. active proteins, immersed in a passive fluid \cite{3}. We use it to study the membrane conformation fluctuations and the associated active or nonequilibrium MPTs. Both second order MPT (through critical and tricritical points), and first order MPT are considered. We uncover

\footnote{4 It discusses a study on protein pumps in a fluid membrane; the membrane in this work, however, is asymmetric under inversion, and hence different from ours.}
a direct correspondence between membrane fluctuations and the nature of the MPTs, potentially opening up a new experimental route to study the MPTs. Our predictions are quite general; we expect that our characterisations of the membrane fluctuations and MPTs should serve as references for experimental observations on MPTs in mixed model bilayers and GPMVs in isotropic actomyosin extracts with adenosine triphosphate (ATP) molecules or solutions of live orientable bacteria [13], and lipid membranes with active protein inclusions embedded in passive fluids. From perspectives of nonequilibrium physics, our model provides an intriguing example where the same underlying microscopic active processes control two distinct phenomena, viz. MPTs of the membrane composition and the nature of fluctuations of the membrane conformation, ultimately linking the two in a definitive way.

In order to focus on the essential physics of the problem, we consider a planar, tensionless, two-component, inversion-symmetric\(^5\), single-layered lipid membrane\(^6\), of linear size \(L\). In stark contrast to equilibrium lipid membranes\([15, 16]\), our model membrane displays generic stiffening and statistical flatness for positive active tensions \(\sigma_0\), but softening and crumpling for \(\sigma_0 < 0\) at any temperature \(T\). We describe the planar membrane conformations by a single-valued height field \(h(x, t)\) in the Monge gauge\([9, 17]\), in two-dimensions (2D) with the local normal \(\mathbf{n} = (-\nabla h, 1) = (\delta n_1, 1)\)\([9, 17]\). Then, for positive \(\sigma_0\), away from the critical point for second order MPT and across first order MPT we find variances

\[
\begin{align*}
\Delta_n &= \langle (\delta n(x, t))^2 \rangle \sim \text{const.}, \\
\Delta_h &= \langle h(x, t)^2 \rangle \sim \ln L,
\end{align*}
\]

in the thermodynamic limit (TL). These imply orientational long range order (LRO), hence statistical flatness and positional quasi long range order (QLRO); here \(\langle \cdot \rangle\) implies averaging over noises; see dynamical equations (8) and (9), respectively, below. Near the critical point, the membrane becomes super stiff; in a mean-field like treatment, we show

\[
\Delta_h \sim \ln \ln L,
\]

in TL, an \(L\)-dependence weaker than in QLRO, which we call positional nearly long range order (NLO). Moreover, \(\Delta_n\) is further suppressed near the critical point. In contrast, for \(\sigma_0 < 0\), \(\Delta_n\) and \(\Delta_h\) diverge for membranes larger than a persistence length, i.e. \(L > \zeta\)\([16]\), indicating orientational and positional short range orders (SRO). The rest of this article is organised as follows. In section 2, we set up our coarse-grained equations of motion. Then in section 3 we discuss our results on the membrane conformation fluctuations at or across various MPTs. Section 4 discusses the various MPTs possible within our model. Finally, in section 5 we summarise our results. A glossary of our results has been added in section 6 for the convenience of the readers. Some technical aspects of the calculations involved and a few additional discussions related to the main results of this work are made available in appendices A–G for interested readers.

2. Construction of the model

We consider an incompressible mixed permeable membrane composed of two lipids \(A\) and \(B\) of equal amount with local concentrations \(n_A(x, t)\) and \(n_B(x, t)\), respectively\([16]\), \(n_A + n_B = 1\). The local inhomogeneity \(\phi(=n_A - n_B)\) is the order parameter for the MPT. Since the active processes may in general interact differently with \(A\) and \(B\), we relax the usual inversion symmetry of \(\phi\) for a binary mixture\([18]\) when coupled to local mean curvatures in the present model (see\([16, 19, 20]\)\(^7\) in this context).

Now, consider a nearly flat permeable membrane spread parallel to the \(xy\)-plane, i.e. with local normals parallel to the \(z\)-axis on average; see figure 1 for a schematic diagram. While the height field \(h\) is a nonconserved broken symmetry variable, the order parameter field \(\phi\) is a conserved density, since \(n_A\) and \(n_B\) are conserved. The relevant equations of motion for \(h\) and \(\phi\) may be derived as follows. The membrane, treated as a permeable fluid film\([21]\), has a local velocity in the normal direction (along \(z\) direction in this case) \(v_{\text{mic}}\) given by

\[
v_{\text{mic}} = v_{\text{hydro}} + v_{\text{perm}}.\]

Here, \(v_{\text{hydro}}\) is the \(z\)-component of the local three-dimensional (3D) hydrodynamic velocity \(v_{\text{hydro}}\)\([12]\), and \(v_{\text{perm}}\) represents the local permissive flows\([12]\). In general, both \(v_{\text{perm}}\) and \(v_{\text{hydro}}\) may contain equilibrium (controlled by a free energy \(\mathcal{F}\); see below) and active parts. The latter contributions cannot be obtained from \(\mathcal{F}\). Instead, symmetry considerations (e.g. translation, in-plane rotation, inversion symmetry of \(h\) and invariance under tilt for the membrane) may be used to enforce the general forms of the active contribution to \(v_{\text{perm}}\). We write

\(^5\) In vitro model lipid bilayers are typically inversion-symmetric; see\([6]\).

\(^6\) We ignore the bilayer structure see e.g.\([14]\).

\(^7\) Actin filaments are known for lipid-specific interactions, e.g. phosphatidylinositol bisphosphate lipids promote actin polymerisation on the membrane; see, e.g.\([1]\).

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\(\text{2}^{nd} \text{line}\)
to the lowest order in nonlinearities and gradients satisfying the relevant invariances. The first term on the rhs of (5) with coefficients \( \lambda \) and \( \tilde{\lambda} \) is the active contribution to \( v_{\text{perm}} \); \( \mu_p \) is a (constant) kinetic coefficient for the equilibrium contribution to the permeative flows. The active terms with coefficients \( \lambda \) and \( \tilde{\lambda} \) are forbidden in equilibrium due to the tilt invariance of the associated free energy \( F \) (see below) [16]. They are, however, permitted here as the tilt invariance in the present problem must hold at the level of the equations of motion [11]. All of \( \lambda, \tilde{\lambda}, \mu_p \) vanish for impermeable membranes. Furthermore, \( \lambda \) and \( \tilde{\lambda} \) control the strength of the active tension (see below); a non-zero \( \tilde{\lambda} \) models the asymmetric dependence of the active processes on lipids A and B. Symmetry arguments cannot determine the signs of \( \lambda, \tilde{\lambda} \). In this work, we examine the consequences of both positive and negative \( \lambda \); the sign of \( \tilde{\lambda} \) can be absorbed within the definition of \( \phi \). Further, for a membrane with a fixed background there are no active contributions to \( v_{\text{hydro}} \) that are more relevant than the \( \lambda, \tilde{\lambda} \)-terms above; \( v_{\text{hydro}} = -\Gamma_0 \delta F / \delta h \) with kinetic coefficient \( \Gamma_0 \) being a constant. The dynamics of \( \phi \) should generally follow a conservation law form advection-diffusion equation [8]. To proceed further, we assume \( F \) for a tensionless, mixed lipid membrane to have the simple generic form

\[
F = \int d^d x \left\{ -\frac{\kappa}{2} (\nabla^2 h)^2 + \lambda_0 \phi^3 (\nabla^2 h)^2 + \lambda_2 \phi (\nabla^2 h)^2 + \frac{r}{2} \phi^2 + \frac{1}{2} (\nabla \phi)^2 + \frac{g}{3} \phi^4 + \frac{u}{4!} \phi^4 + \frac{\nu}{6} \phi^6 - \tilde{h} \phi \right\}.
\]  

(6)

Here \( r = T - T_c, u, \nu > 0 \). Couplings \( g \) and \( \tilde{h} \) can be of either sign; for a symmetric binary mixture \( g = 0 = \tilde{h} \). Coupling \( \nu \) has been added for reasons of thermodynamic stability (see below) and is irrelevant in equilibrium with \( u > 0 \). Free energy (6) without membrane fluctuations \( (h = \text{const.}) \) describes MPTs identical to the standard liquid–gas phase transition that is generally first order in nature, and admits a second order MPT at a critical point that can be accessed only by setting \( T = T_c \) and also tuning \( \tilde{h} \) to a critical value (equivalently setting pressure \( p = p_c \), the critical pressure), in analogy with magnetic systems [9]. This analogy can be made more precise by expanding \( F \) about \( \phi = \phi_0 \), with \( \phi_0 \) is chosen such that the \( g \phi^3 \)-term in \( F \) above vanishes. The resulting transformed free energy has the form same as that of the Ising model at a finite external magnetic field \( h_0 \) (related to \( \tilde{h} \) and depends upon the chemical potential and temperature) that has generic first order MPTs (or may show no transitions) if \( h_0 \) is tuned at any general \( T \); furthermore, second order MPT belonging to the 2D Ising universality class is found if both \( T \) and \( h_0 \) are tuned; the corresponding critical point is located in a \( T-h_0 \)-plane at \( r = 0 \) or \( T = T_c \) (in a mean-field description) and \( h_0 = 0 \) [9]. In fact, the path in the temperature—pressure plane of a binary mixture that directly resembles the zero magnetic field path in a magnet (which shows a second order transition) is the one with the density fixed at the critical density, i.e. the critical isochore. Notice that the coexistence curve for \( F \) above is similar to that for the Ising model, except now being asymmetric with respect to the order parameter \( \langle \phi \rangle = m \) due to the lack of any symmetry of \( F \) under inversion of \( \phi \) [9]. The inclusion of \( h \)-fluctuations in (6) via the couplings \( \lambda_1, \lambda_2 \) does not alter this picture [6, 16]. This may be easily
seen from the form of \( \mathcal{F} \): the \( \lambda_1 \) and \( \lambda_2 \) terms effectively only induce fluctuation-correctors to \( r \) and \( \tilde{h} \), respectively. To what degree this equilibrium physical picture is affected by the activity remains to be seen (see below).

Notice that \( \mathcal{F} \) implies an effective composition-dependent bending modulus \( \tilde{k}(\phi) \) of the form [16]

\[
\tilde{k}(\phi) = \kappa + 2\lambda_1 \phi^2 + 2\lambda_2 \phi.
\]

Parameters \( \lambda_1 \), \( \lambda_2 \) should be chosen to ensure \( \tilde{k}(\phi) > 0 \) for all \( \phi \), that guarantees a thermodynamically stable flat phase, given by the minimum of \( \mathcal{F} \), in equilibrium. We choose \( \lambda_1 > 0 \) [16]. The sign of \( \lambda_2 \) is arbitrary and can be absorbed within the definition of \( \phi \); for concreteness we choose \( \lambda_2 > 0 \). While the individual signs of \( \tilde{\lambda} \) and \( \lambda_2 \) are arbitrary, the sign of the product \( \lambda_p \equiv \tilde{\lambda} \lambda_2 \) is crucial to what follows below and controls the ensuing macroscopic behaviour.

Putting together everything, the dynamical equations for \( h \) (with \( \partial_t h = v_{nc} \)) and \( \phi \) to the lowest order in spatial gradient expansions, in the long wavelength limit take the forms (for a fixed background medium)

\[
\frac{\partial h}{\partial t} = \Gamma_h [-\kappa \nabla^2 h + (\lambda_1 \phi^2 + \tilde{\lambda} \phi) \nabla^2 h] + f_h,
\]

\[
\frac{\partial \phi}{\partial t} = \Gamma_\phi \nabla^2 \left[ r \phi - \nabla^2 \phi + \frac{u}{3!} \phi^3 + 2\lambda_1 \phi (\nabla^2 h)^2 + \lambda_2 (\nabla^2 h)^2 + \nu \phi^5 \right] + \nabla \cdot F_p.
\]  

Notice that the terms with coefficients \( \lambda_1 \), \( \lambda_2 \) in (6) generate additional equilibrium terms in (8); these are however subleading in the hydrodynamic limit (in a scaling sense) to the active \( \lambda_1 \), \( \tilde{\lambda} \)-terms, respectively, and are hence omitted from (8). Kinetic’ coefficient \( \Gamma_h = \mu_p + \Gamma_{\tilde{h}} \) is a constant for a membrane with a fixed background; \( \Gamma_\phi \) is also a constant. Notice that separately equation (9) may be wholly obtained from \( \mathcal{F} \) and is just of the ‘model B’ conservation law form (in the nomenclature of [8]); this is because there are no active terms which are more relevant (in a scaling sense) than those already included in (9). In fact, the \( \lambda_1 \)- and \( \tilde{\lambda} \)-nonlinear terms in (9) originate from the composition-dependent bending modulus \( \kappa(\phi) \) in (7) in the free energy (6). This does not, however, in general imply that \( \phi \) follows an equilibrium dynamics; its coupling with \( h \) ensures that the resulting effective dynamics for \( \phi \) is detailed balance breaking. Further, we have ignored any in-plane advection of \( \phi \) for simplicity.\(^9\) Noises \( f_h \) and \( f_\phi \) are zero-mean, Gaussian distributed with variances given by

\[
\langle f_h(q, \omega) f_h(q', \omega') \rangle = 2D_h \Gamma_h \delta(q + q') \delta(\omega + \omega'),
\]

\[
\langle f_\phi(q, \omega) f_\phi(q', \omega') \rangle = 2D_\phi \Gamma_\phi \delta(q + q') \delta(\omega + \omega'),
\] 

Here, \( D_h = D_\phi \) in general; \( q, q' \) are wavevectors and \( \omega, \omega' \) are frequencies, \( q = \|q\| \). Noises \( f_h \) and \( f_\phi \) should contain both thermal as well as active contributions.

**2.1. Active terms**

The dynamical equations (8) and (9) are constructed using symmetry arguments. As a result, these serve as good hydrodynamic representations for a variety of systems that conform to the same symmetries as equations (8) and (9). Equivalently, the active terms in (8) can be motivated in various physical contexts. For instance, consider an inversion-symmetric, mixed, planar fluid membrane placed in an isotropic, active suspension of actin filaments [10], grafted normally to it. This is imposed by the condition \( p \cdot n = 1 \), where \( p \) is the local orientation or director fields [23] which describe the local orientation of the actin filaments. This yields \( p_j = \partial_j h (j = x, y) \) to the linear order in height fluctuations [24] at the location of the membrane \( z = h \). In the embedding bulk isotropic active medium, there is no net orientational order and hence the fluctuations of \( p \) relax fast [12]. Thus\(^11\), \( p \) in the bulk are not hydrodynamic variables and can be ignored in the long time limit as far as the bulk embedding fluid is concerned. At \( z = h \), the location of the membrane, however, \( p \) is nonzero and is slaved to the membrane fluctuations, as above. The general form of the \( z \)-component of the local membrane velocity, taking into account the permeative flow, is

\(^9\)To recover the correct equilibrium limit, one needs to drop the \( \lambda_1 \)- and \( \tilde{\lambda} \)-terms in (8) and reinsert the \( \lambda_1 \)- and \( \lambda_2 \)-terms in (8). The absence of the \( \lambda_0 \)- and \( \lambda_4 \)-terms in (8) does not affect our analysis of the active membrane fluctuations in the long wavelength limit.

\(^10\)We do not include active \( \phi^2 \)-, or \( \phi^4 \)-terms. Such terms would survive even for \( h = \) const., where as active processes here are assumed to couple with the membrane via mean curvature \( \nabla^2 h \), and hence all active effects on the membrane should vanish for \( h = \) const. This rules out an active \( \phi^2 \)-term in equation (9). In any case, these are no more relevant (in a scaling sense) than those (of equilibrium origin) already exist in (9).

\(^11\)By this we mean a nonvanishing relaxation rate of \( \Phi \) in the limit of wavevector \( q \rightarrow 0 \).
In general, the dynamical equation for an isolated tensionless fluid membrane at thermal equilibrium. We then establish their correspondence with the generic leading order active terms present for a pure fluid membrane at thermal equilibrium. We can write the active terms in such systems should describe the mole fraction of the active components. The main physical features of these active proteins are that they force the membrane locally and independently of each other, generating a local normal motion of the membrane that should evidently depend upon \( \phi \). The active terms in (8) then simply model the \( \phi \)-dependence of the local normal velocity of the membrane. This \( \phi \)-dependence leads to the active tension \( \sigma_{\phi} \); see below.

Now imagine regions of nonzero mean curvature with excess lipid of one kind so that \( \phi \) picks up a non-zero value with a specific sign. Such a region then either pulls up the curved region further (instability) or tries to flatten the curvature (stable membrane) due to the active processes; see figure 2 for a schematic picture. For an active fluid with actin filaments, \( \lambda, \tilde{\lambda} \) should scale with the concentration \( C_0 \) of the ATP molecules and the free energy released in hydrolysis of ATP, \( \Delta \mu \sim 0.8 \times 10^{-18} \text{kJ} \) [28]. In the example of a live cytoskeletal extract, active contributions to \( v_{\text{perm}} \) should depend on the treadmilling speed of the actin filaments \( \sim O(1 \ \mu\text{m} \ \text{s}^{-1}) \) [29]; this may be used to make an estimate on \( \lambda, \tilde{\lambda} \). For a membrane with an active component, \( \lambda, \tilde{\lambda} \) should scale with the mean concentration of the active species in the membrane.

It is now instructive to compare and contrast with the generic leading order active terms present for a pure tensionless membrane (\( \phi = 0 \)). For a pure membrane, the leading order active propulsion velocity is just a constant: \( X(\phi = 0) = \Gamma_0 \alpha \) to the leading order. Thus, for such a pure membrane with a vanishing tension in an active medium, the dynamical equation for \( h \) can be obtained from an effective free energy that now includes an effective surface tension \( \sigma' = \alpha \) in the free energy. We can write

\[
\frac{\partial h}{\partial t} = -\Gamma h \delta F_h / \delta h + v_{\text{hydro}} + f_h,
\]

where \( F_h = \int d^3x \{ \alpha' (\nabla h)^2 / 2 + \kappa (\nabla^2 h)^2 / 2 \} \). Thus, for a symmetric pure membrane, the active effects may be wholly described by a modified equilibrium free energy \( F_h \) to the leading order, or, equivalently, the role of active effects here is to just to introduce an effective surface tension. For a mixed membrane, there is no such general equivalence with a simply modified equilibrium model.

3. Results

In this section we first derive our results on membrane fluctuations without any (equilibrium) surface tension by using the model equation (8). We analyse equation (8) in a mean field-like spirit and compare its properties withiable tensionless fluid membrane at thermal equilibrium. We then establish their correspondence with the
order of MPTs, the principal prediction of this work. Next, we briefly touch upon how a finite surface tension may affect our results. We now proceed to discuss these in details below.

### 3.1. Properties of membrane fluctuations

The lack of knowledge about the order of MPTs in a symmetric mixed membrane embedded in an active fluid, demands that we must allow for the possibility of both first order MPT and second order MPT, and study their connections with the membrane fluctuations separately; see [30] for a recent study of first order MPT in a lipid bilayer in presence of transmembrane proteins. In particular, this opens the intriguing possibility of activity-induced first order MPT in a mixed lipid bilayer that admits only second order MPT in the equilibrium limit. We present theoretical arguments in favour of both first order MPTs and second order MPTs later in the text. From (8), we extract an active tension $\sigma_a$. We write in the Fourier space

$$\frac{\partial h}{\partial t} = \Gamma h [ - \kappa q^4 h - X(\phi) q^2 h] + f_h, \tag{14}$$

where $X(\phi) = \lambda \phi^2 + \bar{\lambda} \bar{\phi}$; $q$ is a Fourier wavevector. Now write $X(\phi) = \langle X(\phi) \rangle + \delta X(\phi)$; $\delta X(\phi)$ is the fluctuation of $X(\phi)$ about its mean $\langle X(\phi) \rangle$. Then, neglecting $\delta X(\phi)$ in comparison with $\langle X(\phi) \rangle$ for (assumed) small fluctuations (in mean-field like treatment) and for any $\lambda \neq 0$, we can extract an active tension $\sigma_a$ as follows:

$$\sigma_a = \lambda \langle \phi^2 \rangle, \tag{15}$$

with $\langle \phi \rangle = 0$ for the whole system with equal $A$ and $B$ at all $T$; clearly $\sigma_a$ is positive (negative) for $\lambda > (\lambda < 0)$. Consider $\lambda > 0$ first. Equations (14) and (15) imply for the membrane height fluctuations

$$C_a(q) = \langle |h(q)|^2 \rangle = \frac{D_h}{\sigma_a q^2 + \kappa q^4}. \tag{16}$$

Thus $C_a(q)$ is dominated by the active tension $\sigma_a q^2 > 0$ in the long wavelength limit, since $\kappa q^4$ is subleading to it (in a scaling sense). At this stage it is formally instructive to compare $C_a(q)$ as given in (16) with that of a tensionless fluid membrane (since our model membrane has zero surface tension in equilibrium) with an effective bending modulus $\kappa_e$ in equilibrium at temperature $D_h / (1_s K_h)$. This yields

$$\kappa_e(q) = \kappa + \frac{\sigma_a}{q^2} = \kappa + \frac{\lambda}{q^2} \langle \phi^2 \rangle. \tag{17}$$

Unsurprisingly, $\kappa_e(q)$ has a part that diverges as $1/q^2$, a reflection of the active tension $\sigma_a(q)$, that is dimensionally identical to the usual surface tension. Equivalently, to the leading order our tensionless model membrane behaves like an equilibrium membrane under tension. This suggests generic stiffening (softening) of the model membrane for $\lambda > (\lambda < 0)$ at any $T$, in contrast to an isolated fluid membrane in equilibrium [16]. Positive and negative $\lambda$, respectively, physically imply that creation of nonuniform regions with specific signs of $\phi$ (i.e. A- or B-rich domains) should make the membrane either try to flatten out ($\sigma_a > 0$), or curve more ($\sigma_a < 0$); see also [4, 12] (see footnote 3) for active tension in different models for active membranes. Now assume $\lambda > 0$. In the ordered phase, $\langle \phi^2 \rangle = m^2$ (neglecting fluctuations) is larger than its value in the disordered phase; hence $\kappa_e(q) > \kappa$ in the ordered phase, where $m$ is the average of $\phi$ in an $A$- or $B$-rich domain in the ordered phase.

For a putative first order MPT at $T = T^*$, we write

$$\sigma_a(q) = \lambda \langle \phi^2 \rangle \implies \kappa_e(q) = \kappa + \lambda \langle \phi^2 \rangle / q^2 (T > T^*),$$

$$\sigma_a(q) = \lambda m^2 \implies \kappa_e(q) = \kappa + \lambda m^2 / q^2 (T < T^*), \tag{18}$$

ignoring $\phi$-fluctuations in comparison with $m^2$ for $T < T^*$. Thus there is a jump in $\kappa_e$, that is large for small $q$, as $T$ crosses $T^*$. Now,

$$\Delta_h = D_h \int_{2\pi / L}^L \frac{d^2 q_i}{\kappa_e(q_i)^2} \approx \bar{\lambda} \ln L \tag{19}$$

in TL, implying positional QLRO, where, $\bar{\lambda}$ is a nonuniversal constant with a value dependent upon ordered and disordered phases; $\bar{\lambda} = \frac{D_h}{2\pi \lambda m^2}$ (for $T < T^*$); see equation (2). Here, $\mathbf{q}_i$ is a wavevector; $|\mathbf{q}_i| = q_i$; $\Lambda$ is an upper wavevector cut-off. With equation (15),

$$\Delta_a = D_h \int_{2\pi / L}^L \frac{q_i^2 d^2 q_i}{(2\pi)^2 \kappa_e(q_i)^4} \tag{20}$$

is finite in TL (i.e. orientational LRO), independent of the nature of MPTs. Note that both $\Delta_a$, $\Delta_h$ are discontinuous across $T^*$, due to the discontinuity in $\kappa_e(q)$ across first order MPT.

In contrast, for second order MPT $\langle \phi^2 \rangle$ changes continuously on both sides of $T = T_c$ and rises as $|r(T)|$ becomes smaller. Thus $\kappa_e(q)$, as given by (15), rises smoothly as $T_c$ is approached from either side; see figure 3.
For $T > T_c$, 
\[ \kappa_\lambda(q) \approx \frac{\lambda D_0}{4\pi^2q^2} \int_{2\pi/L}^{\lambda} \frac{d^2q_1}{r + q_1^2} = \frac{\lambda D_0}{4\pi^2} \ln \left| \frac{r + \lambda^2}{r} \right|. \]  

(21)

This yields 
\[ \Delta_h = G \ln L \]  

in TL, implying positional QLRO for $T > T_c$; giving equation (2) above; $\tilde{G} = \frac{2D_0}{\lambda D_0 \ln \left( \frac{2\pi}{q_0} \right)}$, a nonuniversal constant, different from $\tilde{\lambda}$. For $T < T_c$ as well, positional QLRO holds, however, with a different nonuniversal value for $G$. For both $T > T_c$ and $T < T_c$,  
\[ \Delta_n = \int_{2\pi/L}^{\lambda} \frac{d^2q}{(2\pi)^2} \frac{D_h}{\kappa_\lambda q^2} \]  

remains finite in TL. However, unlike for first order MPT, both $\Delta_n$ and $\Delta_h$ are continuous across $T_c$ for second order MPT. Variations of $\kappa_\lambda(q)$ around first order MPT and second order MPT for a given $q$ are shown schematically in figure 3; also see Glossary at the end summarising our results on $\kappa_\lambda(q)$, $\Delta_n$, $\Delta_h$ across MPTs.

Care must be taken while analysing the membrane fluctuations close to the critical point: large $\phi$-fluctuations very close to the critical point should qualitatively change $\sigma_\lambda(q)$ and hence $\kappa_\lambda(q)$. For simplicity, set $\tilde{\lambda} = 0 = \lambda_1$, such that the Ising symmetry for $\phi$ is restored. This suffices for our purposes here, since we are interested in second order MPT only. From (15) with $\lambda > 0$ and within a linearised approximation to equation (9), we find near the critical point ($r \approx 0$) 
\[ \sigma_\lambda(q) = -\frac{\lambda D_0}{2\pi} \ln q \]

\[ \Rightarrow \kappa_\lambda(q) = \kappa - \frac{\lambda D_0}{2\pi q^2} \ln q \approx -\frac{\lambda D_0}{2\pi q^2} \ln q, \]  

(24)

for small $q_1$ see appendix for a renormalised version of equation (24). Then, 
\[ \Delta_n = -\frac{D_h}{\lambda D_0} \int_{2\pi/L}^{\lambda} \frac{d^2q}{(2\pi)^2} \frac{q_1^2}{\kappa_\lambda q^2} \sim \text{finite} \]  

(25)

and 
\[ \Delta_h = (D_h/\lambda D_0) \ln \ln L \]  

(26)

in TL. This establishes orientational LRO and positional NLO, respectively, with $D_h/(\lambda D_0)$ as the nonuniversal amplitude; see equation (6). Thus at $T_c$, $\Delta_h$ is further suppressed from its value at $T = T_c$, yielding a super-stiff membrane at the critical point. This result holds with or without the ambient fluid hydrodynamics. A schematic phase diagram in the $\lambda-T$ plane is shown in figure 5. These are in stark contrast with their equilibrium results. In equilibrium $\Delta_n$ scales as $\ln \ln L$ at $T = T_c$ [16], displaying orientational NLO; at all other $T$, a pure membrane in equilibrium does not remain flat at large scales [16].
For \( \lambda < 0 \), we have \( \sigma_0 < 0 \). Hence \( \kappa_s(q) < 0 \) for sufficiently low \( q \), implying long wavelength instability for planar membranes or occurrence of membrane crumpling. In general, larger \( \langle \phi^2 \rangle \) in the ordered phase leads to a smaller \( \kappa_s(q) \). We define a persistence length \( \zeta \), such that for \( q = 2\pi/\zeta, \kappa_s(\zeta) = 0 \) [16, 31]. This clearly indicates instability of flat membranes, and as argued in [15], the membrane gets crumpled. Physically, for length scales \( L < \zeta \) the membrane appears flat on average, where as for \( L > \zeta \), it is crumpled. The strong dependence of \( \kappa_s \) on the nature of the transition (first order MPT or second order MPT) is also reflected in \( \zeta \). In particular, across an first order MPT at \( T^* \),

\[
\zeta = 2\pi \sqrt{\frac{R}{|\lambda|\langle \phi^2 \rangle}}, \text{ for } T > T^* \quad \text{and}
\zeta = 2\pi \sqrt{\frac{R}{|\lambda|m^2}}, \text{ for } T < T^*,
\]

thus showing a jump in \( \zeta \) in general \( \zeta(T > T^*) > \zeta(T < T^*) \). In contrast, there is no discontinuity in \( \zeta \) for second order MPT at \( T = T_c \); \( \zeta \) satisfies

\[
\zeta^4 \ln(\zeta/(2\pi)) = \frac{8\pi^2 \kappa}{D_\| m}
\]

at \( T_c \). Away from \( T = T_c, \zeta(T > T_c) > \zeta(T < T_c) \), similar to the behaviour of \( \zeta \) across \( T = T^* \) in first order MPT. Both \( \Delta_n \) and \( \Delta_s \) diverge at finite \( L \sim \zeta \), implying orientational and positional SRO. Due to the large fluctuations of \( \phi \) at the critical point, \( \zeta(T_c) \ll \zeta(T = T_c) \), giving super-crumpling of the membrane, in contrast to super stiffness for \( \lambda > 0 \) at the critical point; see appendix for more details.

3.2. Correspondence between membrane fluctuations and order of MPTs—experimental implications

Consider now the implications of the above results on the measurements of membrane conformation fluctuations. These may be measured by standard spectroscopic methods, see, e.g. [32]. Notice that the knowledge of the behaviour of \( \sigma_0 = \lambda \langle \phi^2 \rangle \), or \( \kappa_s(q) \equiv \kappa + \lambda \langle \phi^2 \rangle/q^2 \) immediately enables us to find the scaling of \( C_q(q) = D_h/(\sigma_0 q^2 + \kappa q^4) \) across second order MPT or first order MPT, that can be measured in experiments. We make the following general conclusions:

(i) With second order MPT at both \( T > T_c \) or \( T < T_c \), \( C_q(q) \sim 1/q^4 \) for large \( q \), where as \( C_q(q) \sim 1/q^2 \) for small \( q \) and \( \lambda > 0 \); \( C_q(q) \) diverges for \( q \to 0 \) only with no finite wavevector singularities. Further, since \( \sigma_0(T > T_c) > \sigma_0(T < T_c), C_q(q)(T < T_c) < C_q(q)(T > T_c) \) for sufficiently small \( q \), when \( \sigma_q q^2 \) dominates over \( \kappa q^4 \). Furthermore, the difference \( C_q(q)(T > T_c) - C_q(q)(T < T_c) \) vanishes as \( T \to T_c \), i.e. \( C_q(q) \) has no discontinuity as a function of \( T \), in agreement with the continuity of \( \sigma_0 \) or \( \kappa_s \) across \( T_c \).

(ii) In contrast, for \( \lambda < 0 \) and with second order MPT, \( C_q(q)(T < T_c) > C_q(q)(T > T_c) \). In addition, \( C_q(q) \) diverges at a finite wavevector \( q \sim 2\pi/\zeta \). Nonetheless, \( C_q(q) \) remains continuous across \( T = T_c \), even with \( \lambda < 0 \). These results are summarised in the form of schematic figures in figure 4.

(iii) In case of first order MPT, \( C_q(q)(T > T^*) < C_q(q)(T > T^*) \) with \( \lambda > 0 \), and \( C_q(q)(T < T^*) \) diverges across second order MPT or first order MPT, the difference \( C_q(q)(T > T^*) - C_q(q)(T < T^*) \) does not vanish as \( T \to T^* \). Thus, \( C_q(q) \) is discontinuous across \( T = T^* \), a consequence of the discontinuity of \( \sigma_0 \) or \( \kappa_s \). Qualitatively, the behaviours across the transition temperature \( T^* \) are similar to those for second order MPTs.

The changes in the membrane conformations with \( \lambda \), characterised by \( \Delta_n, \Delta_s \) at a fixed \( T \) may be viewed as a nonequilibrium structural phase transition between soft and stiff phases (see figure 5). An order parameter for this transition may be constructed as in [16, 31].

3.3. Effects of a finite surface tension

If the membrane has a finite surface tension \( \sigma > 0 \), then it generically suppresses \( h \)-fluctuations. Equation (8), in the presence of a finite surface tension \( \sigma \), now modifies to

\[
\frac{\partial h}{\partial t} = \Gamma_h[-\kappa \nabla^4 h + (\sigma + \lambda \phi^2 + \tilde{\lambda} \phi) \nabla^2 h] + f_h.
\]

The equilibrium terms (29) can obtained from the free energy \( F \), now supplemented by contributions from \( \sigma \). Extracting an active tension \( \sigma_0 \) from (29) using the logic outlined above, we find that the dynamics is controlled by the total tension \( \sigma_{tot} \) that includes both the active tension and \( \sigma \),

\[
\sigma_{tot} = \sigma + \sigma_0 > (\cdot \cdot \cdot \sigma_0 > (\cdot \cdot \cdot 0,
\]

\( 0 \).
where \( \sigma \) is defined as in equation (15). A positive \( \sigma_{\text{tot}} \) \( (\lambda > 0) \) necessarily suppresses membrane fluctuations. Thus, for \( \sigma > 0 \), the role of a non-zero \( \sigma \) is to suppress membrane fluctuations further. For \( \sigma < 0 \) \( (\lambda < 0) \), crumpling instabilities should set in only when \( q \to 0 \) for both \( T > T_c \) and \( T < T_c \) (see text). For \( \lambda > 0 \), a positive \( \lambda \) necessarily suppresses membrane fluctuations. For \( \lambda < 0 \), \( \lambda \) diverges only when \( q \to 0 \) for both \( T > T_c \) and \( T < T_c \) phases, respectively. Finite wavevector singularities of \( C_0(q) \) at wavevectors \( q_1 = 2\pi / \zeta_{T > T_c} \) and \( q_2 = 2\pi / \zeta_{T < T_c} \) with \( \zeta \) following equation (38) are visible.

Figure 4. Schematic scaling of \( C_0(q) \) with \( q \) across second order MPTs: (top) \( \lambda > 0 \): red (solid) and blue (broken) curves represents \( C_0(q) \) in the disordered \((T > T_c)\) and ordered \((T < T_c)\) phases, respectively; \( C_0(q) \) diverges only when \( q \to 0 \) for both \( T > T_c \) and \( T < T_c \) (see text). (bottom) \( \lambda < 0 \): red (solid) and blue (broken) curves represents \( C_0(q) \) in the disordered \((T > T_c)\) and ordered \((T < T_c)\) phases, respectively. Finite wavevector singularities of \( C_0(q) \) at wavevectors \( q_1 = 2\pi / \zeta_{T > T_c} \) and \( q_2 = 2\pi / \zeta_{T < T_c} \) with \( \zeta \) following equation (31) are visible.

Figure 5. Schematic phase diagram in the \( \lambda - T \) plane \((\lambda = 0)\). Super-stiff and super-crumpling lines are marked. The solid horizontal (blue) and broken vertical lines refer to \( T = T_c \) and \( \lambda = 0 \), respectively. Symbol \( O \) marks the origin \((0, 0)\).

where \( \sigma \) is defined as in equation (15). A positive \( \sigma_{\text{tot}} \) \( (\lambda > 0) \) necessarily suppresses membrane fluctuations. Thus, for \( \sigma > 0 \), the role of a non-zero \( \sigma \) is to suppress membrane fluctuations further. For \( \sigma < 0 \) \( (\lambda < 0) \), crumpling instabilities should set in only when \( q \to 0 \) for both \( T > T_c \) and \( T < T_c \) (see text). For \( \lambda > 0 \), a positive \( \lambda \) necessarily suppresses membrane fluctuations. For \( \lambda < 0 \), \( \lambda \) diverges only when \( q \to 0 \) for both \( T > T_c \) and \( T < T_c \) phases, respectively. Finite wavevector singularities of \( C_0(q) \) at wavevectors \( q_1 = 2\pi / \zeta_{T > T_c} \) and \( q_2 = 2\pi / \zeta_{T < T_c} \) with \( \zeta \) following equation (38) are visible.

Figure 4. Schematic scaling of \( C_0(q) \) with \( q \) across second order MPTs: (top) \( \lambda > 0 \): red (solid) and blue (broken) curves represents \( C_0(q) \) in the disordered \((T > T_c)\) and ordered \((T < T_c)\) phases, respectively; \( C_0(q) \) diverges only when \( q \to 0 \) for both \( T > T_c \) and \( T < T_c \) (see text). (bottom) \( \lambda < 0 \): red (solid) and blue (broken) curves represents \( C_0(q) \) in the disordered \((T > T_c)\) and ordered \((T < T_c)\) phases, respectively. Finite wavevector singularities of \( C_0(q) \) at wavevectors \( q_1 = 2\pi / \zeta_{T > T_c} \) and \( q_2 = 2\pi / \zeta_{T < T_c} \) with \( \zeta \) following equation (31) are visible.

Figure 5. Schematic phase diagram in the \( \lambda - T \) plane \((\lambda = 0)\). Super-stiff and super-crumpling lines are marked. The solid horizontal (blue) and broken vertical lines refer to \( T = T_c \) and \( \lambda = 0 \), respectively. Symbol \( O \) marks the origin \((0, 0)\).

where \( \sigma \) is defined as in equation (15). A positive \( \sigma_{\text{tot}} \) \( (\lambda > 0) \) necessarily suppresses membrane fluctuations. Thus, for \( \sigma > 0 \), the role of a non-zero \( \sigma \) is to suppress membrane fluctuations further. For \( \sigma < 0 \) \( (\lambda < 0) \), crumpling instabilities should set in only when \( q \to 0 \) for both \( T > T_c \) and \( T < T_c \) (see text). For \( \lambda > 0 \), a positive \( \lambda \) necessarily suppresses membrane fluctuations. For \( \lambda < 0 \), \( \lambda \) diverges only when \( q \to 0 \) for both \( T > T_c \) and \( T < T_c \) phases, respectively. Finite wavevector singularities of \( C_0(q) \) at wavevectors \( q_1 = 2\pi / \zeta_{T > T_c} \) and \( q_2 = 2\pi / \zeta_{T < T_c} \) with \( \zeta \) following equation (38) are visible.

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where \( \sigma \) is defined as in equation (15). A positive \( \sigma_{\text{tot}} \) \( (\lambda > 0) \) necessarily suppresses membrane fluctuations. Thus, for \( \sigma > 0 \), the role of a non-zero \( \sigma \) is to suppress membrane fluctuations further. For \( \sigma < 0 \) \( (\lambda < 0) \), crumpling instabilities should set in only when \( q \to 0 \) for both \( T > T_c \) and \( T < T_c \) (see text). For \( \lambda > 0 \), a positive \( \lambda \) necessarily suppresses membrane fluctuations. For \( \lambda < 0 \), \( \lambda \) diverges only when \( q \to 0 \) for both \( T > T_c \) and \( T < T_c \) phases, respectively. Finite wavevector singularities of \( C_0(q) \) at wavevectors \( q_1 = 2\pi / \zeta_{T > T_c} \) and \( q_2 = 2\pi / \zeta_{T < T_c} \) with \( \zeta \) following equation (38) are visible.

Figure 5. Schematic phase diagram in the \( \lambda - T \) plane \((\lambda = 0)\). Super-stiff and super-crumpling lines are marked. The solid horizontal (blue) and broken vertical lines refer to \( T = T_c \) and \( \lambda = 0 \), respectively. Symbol \( O \) marks the origin \((0, 0)\).

where \( \sigma \) is defined as in equation (15). A positive \( \sigma_{\text{tot}} \) \( (\lambda > 0) \) necessarily suppresses membrane fluctuations. Thus, for \( \sigma > 0 \), the role of a non-zero \( \sigma \) is to suppress membrane fluctuations further. For \( \sigma < 0 \) \( (\lambda < 0) \), crumpling instabilities should set in only when \( q \to 0 \) for both \( T > T_c \) and \( T < T_c \) (see text). For \( \lambda > 0 \), a positive \( \lambda \) necessarily suppresses membrane fluctuations. For \( \lambda < 0 \), \( \lambda \) diverges only when \( q \to 0 \) for both \( T > T_c \) and \( T < T_c \) phases, respectively. Finite wavevector singularities of \( C_0(q) \) at wavevectors \( q_1 = 2\pi / \zeta_{T > T_c} \) and \( q_2 = 2\pi / \zeta_{T < T_c} \) with \( \zeta \) following equation (38) are visible.

Figure 5. Schematic phase diagram in the \( \lambda - T \) plane \((\lambda = 0)\). Super-stiff and super-crumpling lines are marked. The solid horizontal (blue) and broken vertical lines refer to \( T = T_c \) and \( \lambda = 0 \), respectively. Symbol \( O \) marks the origin \((0, 0)\).
4. Nature of MPTs

There is no general framework available to study phase transitions in nonequilibrium systems. Nonetheless we are able to analyse the MPTs here by drawing analogy between the effective theory for composition fluctuations and standard equilibrium results.

Regardless of the nature of MPTs, we have for a symmetric membrane $\langle \nabla^2 h \rangle = C = 0$. Now, ignoring height fluctuations, if we substitute $\nabla^2 h$ by $C = 0$ in (9), it reduces to the standard equilibrium, conserved dynamics (model B in the nomenclature of [8]), corresponding to the free energy (6) [with $h = \text{const.}$] that yields phase behaviour identical to the standard liquid gas transition at temperature $D$, phase coexistence for $r < 0$ or $T < T_c$ with an asymmetric coexistence curve about the critical density and a critical point at $T = T_c$ belonging to the 2D Ising universality class [9]. Thus any active modification of this equilibrium-like picture should be fluctuation induced. To investigate that further, we follow [33] and perturbatively integrate out $h$-fluctuations and obtain an effective dynamical equation for $\phi$ only. Operationally, to account for the fluctuation effects at the simplest level, we calculate the effective (fluctuation-corrected) parameters of (9) at the lowest order in perturbative expansions. We then express (9) in terms of the fluctuation-corrected parameters and substitute $\nabla^2 h$ by $\langle \nabla^2 h \rangle = 0$, ignoring fluctuations. In this approximation, the $\phi$-dynamics is entirely described by a fluctuation-corrected free energy $F_\phi$ entirely decoupled from $h$ which has the form

$$F_\phi = \int d^d x \left[ \frac{r}{2} \phi^2 + \frac{g_e}{3} \phi^3 + \frac{u_e}{4} \phi^4 + \frac{v}{6} \phi^6 - \hat{h} \phi \right],$$

(32)

with

$$\frac{\partial \phi}{\partial t} = \Gamma_\phi \nabla^2 F_\phi + \nabla \cdot \mathbf{f}_\phi$$

(33)

as the attendant effective dynamical equation for $\phi$. In (32), $u_e$ and $g_e$ include only loop corrections to the bare couplings $u$ and $g$, respectively. Here we have ignored the corrections to $r$ and $v$ since these are not central to the analysis here; a correction to $r$ merely shifts $T_c$ and we assume $v$ is always positive. Further, $\hat{h}$ has no active corrections at the lowest order. Thus the one-loop effective dynamics of $\phi$ follows the equilibrium model B dynamics with free energy $F_\phi$ at an effective temperature $D_\phi$.

With $\lambda > 0$, retaining only the inhomogeneous active one-loop correction to $u$ and $g$ (this suffices for our arguments here) we obtain $u_e = u + \Delta u = u + \lambda_g \hat{h} \lambda D h A$ and $g_e = g + \hat{h} \lambda g \lambda D h B$ where, $\lambda_g = \lambda_1 \hat{h}$ and $A$, $B_1$, $B_2$ are numerical constants; see appendix C. Thus effective couplings $u_e$ and $g_e$ can be independently positive, negative or zero.

The phase behaviour and transitions of $\phi$ can be directly obtained from $F_\phi$. First consider $u_e > 0$. The term $v\phi^6$ in (32) is now redundant and we ignore it. Then $F_\phi$ has the same form as $F$ in (6). As a result, the discussions that immediately follow $F$ apply to $F_\phi$ as well: by making a suitable shift in $\phi$, the cubic term $g_e \phi^3$ may be eliminated from $F_\phi$, yielding a modified form for $F_\phi$ identical to the free energy for the Ising model in the presence of an external magnetic field $\hat{h}_\phi$. Then, composition $\phi$ generally undergoes a first order MPT below a transition temperature. A critical point with a second order MPT may be accessed by controlling the activity. The role of $g_e \neq 0$ is only to introduce an asymmetry of the order parameter $\langle \phi \rangle = m$ about the critical density, reflected in the curvature of the coexistence curve at the criticality [9]. Since $g_e$ can be varied continuously and made positive, negative or zero by tuning the composition-membrane interactions parameters, the curvature at criticality and hence the location of the coexistence curve in the $\phi$–$D_\phi$ plane changes continuously with the active parameters. Experimental measurements of the coexistence curve for a given system can thus reveal valuable quantitative information about the active coefficients and the underlying active processes in the membrane.

To ensure thermodynamic stability for $u_e < 0$, we need to include the $v\phi^6$-term into consideration. This then yields a first order MPT at temperature $T' = T_c + 2u_e^2 / (3v)$ and $m' = |u_e| / (2v)$ even for $h_\phi = 0$ in direct analogy with the known equilibrium MF results [9]. At the tricritical point, $u_e = 0$, i.e. $u = - \lambda_g \hat{h} \lambda D h A$ and $\hat{h}_c = 0$. Notice that, unlike equilibrium examples of tricritical points [9], here the condition for the tricritical point explicitly involves $D_\phi$, thus bearing the hallmark of nonequilibrium [34]. While the MPTs for $u_e > 0$ are essentially indistinguishable from their equilibrium counterparts or the equilibrium liquid–gas phase transitions with a second order MPT accessible by setting $\hat{h}_\phi = 0$ and tuning $T$ to $T_c$, the prospect of a first order MPT for $u_e < 0$ at $\hat{h}_\phi = 0$ at $T = T^* > T_c$ and the associated tricritical point are truly remarkable in that they have no analogues in the equilibrium limit of the MPTs or in the equilibrium liquid–gas phase transition.
Fluctuation induced shifts in $T_\text{c}$ and $T^*$ due to $\lambda_p = 0$ are argued to be finite (see appendix), suggesting $T_\text{c}$ and $T^*$ to be experimentally accessible at least for certain inversion-symmetric mixed membranes with proper choices for the model parameters. A schematic phase diagram of the model in the $\lambda_p-u$ plane with $\lambda > 0$ and $\tilde{h}_0 = 0$ is shown in figure 6. Our analysis of MPTs are only indicative in nature that may be confirmed by detailed numerical studies.

5. Summary and outlook

We have thus developed an active hydrodynamic theory for inversion-symmetric mixed membranes. There may be a variety of physical realisations which may be described by our model in the hydrodynamic limit, e.g. a mixed symmetric lipid membrane immersed in an isotropic active fluid or a mixed symmetric lipid membrane with an active component in a passive fluid. We demonstrate that the interplay between heterogeneity and the active processes in the form of lipid-dependent active tensions leads to nontrivial fluctuation properties of mixed membranes. We establish a direct correspondence between membrane conformation fluctuations and MPTs in mixed lipid membranes, which forms a key result of this work. This can be tested in in vitro experiments on various physical realisations of our model; membrane fluctuations may be measured by spectroscopic methods [32]. In particular, tagged particle diffusion measurements [7] may be used to validate our results. We welcome construction of lattice-gas type nonequilibrium models which will be particularly suitable to numerically study and verify the results obtained here; see, e.g. [35]. Our work clearly provides a way to ascertain the sign of $\lambda$ and the nature of MPTs without measuring $\phi$-fluctuations. For a jump in $\sigma_\text{d}$ or $\kappa_\text{d}$ at a given $T = T^*$, it must be first order MPT; else if $\sigma_\text{d}$ or $\kappa_\text{d}(q)$ rises smoothly and diverges at some $T = T_\text{c}$, as $q \to 0$, the system displays second order MPT. Furthermore, if $\sigma_\text{disorder} < (>) \sigma_\text{order}$, or equivalently, $\kappa_\text{disorder} < (>) \kappa_\text{order}$, then $\lambda > (<) 0$. A mixed lipid membrane immersed in an active isotropic fluid made of actin filaments is a possible in vitro system to study our theory. This may be possible by reconstituted actomyosin arrays on a liposome; see, e.g. [36] for a related experimental study. ATP depletion methods [37] can be used to control the magnitude of $\lambda$ and $\tilde{\lambda}$. It would be interesting to see how contractile or extensile active fluids [10] affect the couplings $\lambda$, $\tilde{\lambda}$. The sign of $\lambda_p$, crucial in our theory for fixing the order of MPT, may be varied by using different sets of lipids. It may be noted that in the ordered phase separated state with $A$- and $B$-rich domains, one may define a $\kappa_\text{d}$ in a given domain that is $A$- or $B$-rich. Measurement of this domain-dependent $\kappa_\text{d}$ can further yield information about both $\lambda$, $\tilde{\lambda}$ see appendix.

So far in the above, we ignored hydrodynamic friction [22]. Even when that is included in our analysis, our general conclusion of a one-to-one correspondence between the membrane conformation fluctuations and the nature of the MPTs holds good. Interestingly with hydrodynamic friction, our results hold true even if the membrane is impermeable, i.e. $v_\text{perm} = 0$; see appendix. We have neglected the geometric nonlinearities in our analysis above. These originate from the nonlinear forms of the area element and mean curvature in the Monge gauge; see [17]. These are irrelevant near the critical point in a scaling sense in the presence of the existing nonlinearities. Across first order MPT these may affect the first order transition temperature $T^*$ and order parameter $m$ quantitatively; however, our general conclusions are expected to remain unchanged. Beyond its immediate applicability to suitable in vitro systems, our theory should serve as a basis for studying the physics of phase transitions in live cell membranes. We expect our theory to introduce new directions in the physical understanding of living cell membrane dynamics with new vistas of striking nonequilibrium phenomena. We look forward to experimental tests of our predictions on GPMVs and live cell membrane extracts.
6. Glossary: $\Delta_n$, $\Delta_h$ and $\zeta$ for first order MPT and second order MPT

Below we provide a list of symbols and the principal results that form the basis of this work here.

$$\Delta_h = \int_{2\pi/L}^{\Lambda} \frac{d^2q}{(2\pi)^3} (|h(q, \Omega)|^2), \quad (34)$$

where $\Omega$ is a frequency and $|h(q, \Omega)|^2 = \frac{|\frac{1}{2} \omega(q, \Omega) f_1|}{\tau^2 + \Gamma_1 k q^2} = \frac{2D_h \Omega}{\tau^2 + \Gamma_h k q^2}$. Similarly,

$$\Delta_n = \int_{2\pi/L}^{\Lambda} \frac{d^2q}{(2\pi)^3} q^2 (|h(q, \Omega)|^2), \quad (35)$$

We first assume $\lambda > 0$. The membrane becomes generically stiff for all $T$.

Case I: first order MPT at $T = T^*$, ($\lambda_p < 0$; see main text). At all $T$

(i) $\Delta_n$: finite. $\Rightarrow$ orientational LRO.

(ii) $\Delta_h \sim \ln L \Rightarrow$: positional QLRO.

(iii) Effective bending modulus, $\kappa$, shows a jump across $T^*$: $\kappa_c(T > T^*) < \kappa_c(T < T^*)$.

Case II: second order MPT at $T = T_c$.

For any $T \neq T_c$

(i) $\Delta_n$ is finite and smooth (no jump across $T_c$) $\Rightarrow$: orientational LRO.

(ii) $\Delta_h \sim \ln L \Rightarrow$: positional QLRO.

(iii) At $T = T_c$, $\Delta_n$: finite (orientational LRO), in fact further suppressed than its value at $T = T_c$. On the other hand, $\Delta_h \sim \ln \ln L$ at $T = T_c$ $\Rightarrow$ positional NLO.

(iv) Effective bending modulus, $\kappa$, rises smoothly as $T_c$ is approached.

Now assume $\lambda < 0$: generic crumpling is introduced at all $T$ giving a finite persistence length.

(i) Second order MPT: $\zeta(T < T_c) < \zeta(T > T_c)$; $\zeta(T = T_c) \ll \zeta(T \neq T_c)$, $\zeta(T = T_c)$ follows the equation

$$\zeta^2 \ln(\zeta/2\pi) = \frac{8\pi^2\kappa}{D_h |\lambda|}. \quad (36)$$

(ii) First order MPT: $\zeta(T < T^*) < \zeta(T > T^*)$.

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Appendix A. The active terms

We now briefly discuss a more formal derivation of the active terms. To this end, we closely follow [12], keeping the example in mind of a lipid membrane embedded in an isotropic active fluid made of actin filaments and motors. In the Monge gauge for a nearly planar membrane along the $xy$-plane, we can write for the local membrane velocity $v_z$ as appropriate for a symmetric membrane (set $\sigma = 0$)

$$\frac{\partial h}{\partial t} = v_z = v_{\text{hydro}} + X(\phi) \nabla_j (p_j p) - \Gamma_h \delta F/\delta h. \quad (A1)$$

We use $p_i = \partial h / \partial i$, $i = x, y$ at the location of the membrane; $v_{\text{hydro}}$ is the $z$-component of the 3D hydrodynamic velocity $v_{\text{hydro}}$. This may be formally justified by closely following the arguments outlined in [12]. We assume that the free energy is dissipated at a rate $\mathcal{R} \Delta \mu$, where $\mathcal{R}$ is the reaction rate of ATP hydrolysis and $\Delta \mu$ is as given in the main text. Now treat $v_z$ and $\mathcal{R}$ as fluxes, and $\delta F/\delta h$ and $\Delta \mu$ as the corresponding conjugate thermodynamic forces. Then as in [12], together with the condition for a symmetric membrane, we identify $\bar{\zeta} \nabla_j (p_j p) \delta F/\delta h$ as the leading order contribution to $\mathcal{R}$ up to the first order in gradients, where $\bar{\zeta}$ is an Onsager coefficient. Using the symmetry of the dissipative Onsager coefficients, we then set $\bar{\zeta} \nabla_j (p_j p) = X(\phi) \nabla_j (p_j p)$, giving a justification of the active terms.
Appendix B. Effective bending modulus

In general, from equation (8) (after neglecting fluctuations $\delta X(\phi)$ w.r.t. the mean value $\langle X(\phi) \rangle$), we obtain

$$\sigma_a = \lambda \langle \phi^2 \rangle + \tilde{\lambda}(\phi), \quad \text{or,} \quad \kappa_4(q) = \kappa + \frac{\lambda}{q^2} \langle \phi^2 \rangle + \frac{\tilde{\lambda}}{q^2} \langle \phi \rangle. \quad (B1)$$

We have $\langle \phi \rangle = 0$, considering the whole system with equal amount of $A$ and $B$ lipids in the system. Now, the ordered phase is characterised by finite (macroscopic) size domains, which are $A$-rich or $B$-rich, for $T < T_c$ (second order MPT) or $T < T^*$ (first order MPT). This allows us to define $\sigma_a$ or $\kappa_4$ over a single (macroscopic size) domain, either $A$ or $B$ rich with average of $\phi$ in a given type of domain being non-zero; $\sigma_a$ (or, $\kappa_4$) will now depend explicitly on the domain type. We now define domain-dependent active tensions $\sigma^A_a$ and $\sigma^B_a$ for $A$- and $B$-rich domains in the ordered phase and find

$$\sigma^A_a = \lambda \langle \phi^2 \rangle_A + \tilde{\lambda}(\phi)_A, \quad \sigma^B_a = \lambda \langle \phi^2 \rangle_B + \tilde{\lambda}(\phi)_B. \quad (B2)$$

Here, $\langle \ldots \rangle_{A,B}$ represents averages taken in an $A$ or $B$ rich domain, respectively. For simplicity, let us consider just two macroscopic size domains, one $A$-rich and another $B$-rich. Within a simple mean-field like description, we define an $A$ ($B$) rich domain formally by $\langle \phi \rangle_A = m > 0$ ($\langle \phi \rangle_B = -m < 0$) and set $\tilde{\lambda} > 0$, $\lambda > 0$. Evidently, for sufficiently large $\lambda$, $\sigma^A_a < 0$. One may then define a threshold $\tilde{\lambda}_c$, given by $\sigma^A_a = 0$. This yields that a crumpling instability takes place in the $B$-rich domain for $\tilde{\lambda} > \tilde{\lambda}_c$, for a given size of the $B$-rich domain, where as $\sigma_a$ remains positive in the $A$-rich domain and thus, the latter should be statistically flat. This is testable in experiments. In contrast, with $\lambda < 0$, the crumpling instability in the $A$-rich domain in the ordered phase may be suppressed by a sufficiently large $\lambda$, such that $\sigma^A_a > 0$ even with $\lambda < 0$. This corresponds to a novel situation, where a large enough flat mixed membrane as a whole is unstable in the disordered phase (since $\lambda < 0$), but a macroscopic part of it (i.e. the $A$-rich domain) gets stabilised and shows statistical flatness in the ordered phase (large $\tilde{\lambda} > 0$). Again, this should be testable in standard experiments. Overall we conclude that the stability and flatness of the mixed membrane, both in the disordered and ordered phases, depend very sensitively on the active processes. Since there are no domains in the disordered phase, the term with coefficient $\tilde{\lambda}$ has no effect on $\sigma_a$ in the disordered phase, independent of first order MPT or second order MPT. Thus, the sign of $\sigma_a$ is necessarily controlled by $\lambda$ in the disordered phase and our results in main text directly apply. For sufficiently small $\tilde{\lambda}$, note that the results do not change qualitatively, and equation (15) remains valid in each domain.

Appendix C. Analysis of the MPTs: active inhomogeneous fluctuation corrections to $u$ and $g$

We begin with the generating functional $[38] \mathcal{Z}$ corresponding to the equations of motion (8) and (9). We find

$$\mathcal{Z} = \int \mathcal{D}h \mathcal{D}\hat{h} \mathcal{D}\phi \mathcal{D}\hat{\phi} \exp(S), \quad (C1)$$

where the action functional

$$S = \int d^2x \left[ \frac{\partial h}{\partial t} - \frac{\partial \hat{h}}{\partial t} + \frac{\lambda}{\tilde{\lambda}} (\nabla^4 h - \lambda \phi^2 \nabla^2 h - \tilde{\lambda}_c \phi \nabla^2 h) + \phi \left[ -\frac{D_\phi \nabla^2}{\Gamma_\phi} \right] \phi - \frac{\mu}{3!} \phi^3 + 2\lambda_0 \phi (\nabla^2 h)^2 + \lambda_2 (\nabla^2 h)^2 + u \phi^4 + v \phi^6 \right]. \quad (C2)$$

One can then formally integrate out $h$ and $\hat{h}$, and define an effective action functional $S_\phi$ as follows:

$$\exp(S_\phi) = \int \mathcal{D}h \mathcal{D}\hat{h} \exp(S). \quad (C3)$$

To evaluate $S_\phi$, we proceed perturbatively and then extract $F_\phi \mathcal{Z}$, such that the effective $\phi$-dynamics is now given by equation (32). Ignoring the fluctuation corrections of $\Gamma_\phi$ and $D_\phi$, as these are not central to the discussion here, we find

$$F_\phi = \int d^2x \left[ \frac{\alpha_1}{2} \phi^2 + \frac{\alpha_2}{2} (\nabla \phi)^2 + \frac{\alpha_3}{3} \phi^3 + \frac{\mu_4}{4} \phi^4 + \frac{\nu_6}{6} \phi^6 \right], \quad (C4)$$

where a subscript $\epsilon$ refers to fluctuation-corrected parameters. The corresponding effective equation of motion of $\phi$ is
In our analysis in the main text, we ignore the difference between $r_e$ and $r_i$, and between $v_e$ and $v_i$, as these are of no significance to the mean-field like arguments used in the main text. We always assume $\nu > 0$. We also ignore the corrections to $D_{\phi}$, since that just changes the effective temperature and is of no direct consequences here. Furthermore, there are no one-loop corrections to $G_{\phi}$, owing to the conservation law form of (9).

To proceed further, we now need to find $g$ and $u$ perturbatively. The lowest order active inhomogeneous fluctuation corrections to $g$ and $u$ may be represented by the following Feynman diagrams; see figures C1, C2 and C3 below.

The correlator function for $h$, written in terms of the effective bending modulus $\kappa_e(q)$, is given by $C_{hh}(q, \Omega) = \mathbb{E}[h(q, \Omega)^2] = \frac{2D_{\phi}^{\lambda} \lambda q^4}{(q^2 + \Omega^2)^2}$. In addition, $G_{\phi}(q, \Omega) = \frac{1}{q^2 + \Omega^2}$ and $G_{h}(q, \Omega) = \frac{1}{q^2 + \Omega^2}$ are the propagators for $\phi$ and $h$, respectively.

Furthermore, we assume $\lambda > 0$ for stability. The one-loop correction, $\Delta u$ (see main text), thus evaluates to the following at 2D:

$$\Delta u = \frac{3\lambda q^2 D_{\phi}}{4} \int_{2\pi/L}^{\Lambda} \frac{d^2 q}{(2\pi)^2} \frac{q^2}{\kappa_e^4 q^6}.$$  

(C6)

Since $\kappa_e(q) = O(1/q^2)$ for sufficiently small $q$, $\Delta u$ is clearly a finite contribution at TL, as argued for in the main text. Similarly, the one-loop correction, $\Delta g$ of $g$, at 2D evaluates to
where, $B_l = \frac{1}{\alpha_l + \Gamma \omega^2}$ and $C_{\phi \phi} = \frac{\partial_\mu b_\phi}{\beta + \Gamma \omega^2}$ are the bare propagator and correlator of $\phi$, respectively.

Figure D1. Relevant one-loop correction to $u$. Here, $G_0^u = \frac{1}{\alpha_l + \Gamma \omega^2}$ is the bare propagator for $u$, $C_{\phi \phi}^0$ and $C_{\phi \phi}$ are as in figure D1.

Figure D2. Total correction to $\lambda$. Here, $G_0^\lambda = \frac{1}{\alpha_l + \Gamma \omega^2}$ is the bare propagator for $\lambda$. $C_{\phi \phi}^0$ and $G_0^\lambda$ are as in Figure D1.

$$\Delta g = \frac{\bar{\lambda}^2 \lambda_2}{2} B_1 + 2 \lambda \lambda_2 B_2,$$

where, $B_1 = \int_{2\pi l / \beta}^{\bar{\lambda}} \frac{d_\omega}{12 + \Gamma \omega^2 + \omega^2 q^2}$ and $\Delta_2 = \int_{2\pi l / \beta}^{\bar{\lambda}} \frac{d_\omega}{12 + \Gamma \omega^2 + \omega^2 q^2}$ are finite in 2D. The sign of $\Delta u$ can thus be varied by varying $\lambda_2$; for sufficiently negative large $\lambda_2$, $u_0$ can be made negative. Similarly, the sign of $\Delta g$ may be varied and may be made positive, negative or zero by tuning $\lambda_2$.

**Appendix D. DRG flow equations and fixed points**

Large critical point fluctuations very close to second order MPT may be systematically handled within dynamic renormalisation group (DRG) frameworks; see [9] for technical details. With $\bar{\lambda} = 0 = \lambda_2$, simple power counting shows that the nonlinear coefficients $\lambda$ and $u$ are equally relevant (in a scaling/DRG sense) at 2D, the physically relevant dimension, with both being marginal at $d = 4$. This calls for a perturbative DRG calculation to be performed on equations (8) and (9), together with an $\epsilon$-expansion, $\epsilon = 4 - d$; see [9]. In this limit, the model admits only second order MPT belonging to the 2D Ising universality class. The one-loop DRG procedure formally involves the following steps (i) obtaining the one-loop fluctuation corrections to the different model parameters by integrating out the high wavevector parts of the fields from $\Lambda / b$ to $\Lambda$, $b > 1$, (ii) rescaling the fields wavevector $q$, frequency $\omega$ by $q' = bq$, $\omega' = b^z \omega$, where $z$ is the dynamic exponent and rescaling of the fields $h$ and $\phi$ accordingly [9]. The fixed points (FP) of the DRG are to be obtained from the flow equations for the relevant coupling constants in the problem, which in the present case are $u$ and $\lambda$. The one-loop diagrams that contribute to $u$ and $\lambda$ are shown below in figures D1 and D2, respectively.

With $b = \epsilon^l \approx 1 + l$, $l \ll 1$, the resulting DRG recursion relations for $u$ and $\lambda$ yield

$$\frac{du}{dl} = u[\epsilon - 9uD_\mu],$$

$$\frac{d\lambda}{dl} = \lambda[\epsilon - 3uD_\mu - 4\bar{\Gamma} \lambda D_\lambda],$$

where $\bar{\Gamma} = \frac{\Gamma_\lambda}{\Gamma_\mu + \epsilon \Gamma_\lambda}$. For the flow equations (D1) and (D2), stable FP $u^\# = \frac{\epsilon}{9D_\mu}$ and $\lambda^\# = \frac{\epsilon}{6\bar{\Gamma} D_\lambda}$. Not surprisingly, $u^\# = \epsilon / (9D_\mu)$ yields the critical exponents for the composition fluctuations at second order MPT identical to...
their values at the Heisenberg FP of the Ising model in equilibrium, consistent with the expectation that the second order MPT belongs to the Ising universality class. At the one-loop order, there are no fluctuation corrections to $\Gamma_0$, $\Gamma_\phi$, $D_\phi$ and $D_\phi$. Now, since we are formally considering a tensionless membrane, noting that the leading order correction to the self-energy of $h(q_1, \omega)$ is at $O(q^4)$, it is convenient to define $\tilde{\kappa}(q) = \kappa q^2$ ($\tilde{\kappa}$ clearly has the physical meaning of a surface tension), and obtain its fluctuation-corrections. We find

$$\frac{d\tilde{\kappa}}{dl} = \frac{\lambda D_\phi}{2\pi}$$

(D3)

as the DRG flow equation for $\tilde{\kappa}$. Solving this at the DRG FP, we obtain a scale-dependent, renormalised $\tilde{\kappa}(q)$ and hence, defining renormalised $\kappa_s(q)$ via $\tilde{\kappa}(q) = \kappa_s(q)q^2$,

$$\kappa_s(q) = \kappa + \frac{\lambda^2 D_\phi}{q^2} \int_q^\lambda \frac{d^2q_1}{(2\pi)^2 q_1^2} \approx -\frac{\lambda^2 D_\phi}{2\pi q^2} \ln q,$$

(D4)

at $d = 2$ for small $q$ at the DRG FP or the critical point ($T = 0$). The one-loop correction to $\kappa$ is shown in figure D3.

Here, at the DRG fixed point $\lambda^2 D_\phi = \epsilon / (6\Gamma)$. Then, $\Delta_\kappa = -\frac{D_\phi}{N\Gamma} \int_q^\lambda \frac{d^2q_1}{\ln q_1}$, where $q_0 \sim 2\pi / L$ is the lower limit of the integral. The nature of the orientational order is determined by the $L$-dependence of $\Delta_\kappa$ in the limit of large $L$ (formally infinite at TL). Whether or not the limit $q_0 \to 0$ may be taken, depends on the behaviour of the integrand, $q_1$ for $q_1 \to 0$. It can be shown in a straightforward way that for $q_1 \to 0$, $q_1 / \ln q_1$ vanishes. Thus, we conclude that for $q_0 \sim 2\pi / L \to 0$, $\Delta_\kappa$ remains finite. A precise numerical value of $\Delta_\kappa$ may be obtained by numerical integrations. This, of course, will depend upon $\lambda$, the upper limit. Since this is not particularly illuminating for the purposes of this work, we do not do this here. Furthermore, $\Delta_\kappa = -\frac{2\pi D_\phi}{N\Gamma} \int_{2\pi / L}^\lambda \frac{d^2q_1}{(2\pi)^2 q_1 ln q_1} \approx \frac{D_\phi}{N\Gamma} \ln L$ in TL. Clearly, the amplitude $D_\phi / (\lambda^2 D_\phi)$ is nonuniversal at the DRG FP and these results are in agreement with results obtained in the main text. Lastly, the lack of renormalisation of $\Gamma_0$ and $\Gamma_\phi$ at the one-loop order implies that dynamic exponent $z = 4$ at second order MPT for both $h$ and $\phi$, respectively (strong dynamic scaling).

Note that similar to $\mu$, $\lambda$ and $\kappa_s$, $r$ also receives fluctuation corrections, reflecting fluctuation-induced shift in $T_c$. Solving the DRG flow equation for $r$ yields the correlation length exponent; see, e.g. [28]. Since this is not central to main issue of this work, we do not discuss this here.

In the above, we have worked up to the one-loop approximation. Notice however that the critical behaviour of $\phi$ follows the Ising universality class as elucidated above, and hence the equal-time correlator of $\phi$ is known exactly near the critical point from the exact solution of the 2D Ising model. We use this below to obtain the temperature-gradient of the renormalised bending modulus $\kappa_\nu(q)$ near the critical point $T = T_c$ (see also [33, 39]). From equation (24), only the equal-time correlator $\langle \phi^2 \rangle$ enters into $\kappa_\nu$, giving [39]

$$\frac{\partial \kappa_\nu}{\partial T} = \lambda \frac{\partial}{\partial T} \langle \phi^2 \rangle \sim -C_v,$$

(D5)

near the critical point. For the 2D Ising model, $C_v \sim \ln((T - T_c)/T_c)$ near $T_c$ yielding a logarithmic divergence [40]. This shows how $\kappa_\nu(q)$ diverges as $T \to T_c$. This in turn yields, upon integrating over temperature, $\kappa_\nu(q)$ has a diverging piece $\propto \ln((T - T_c)/T_c)$ near the critical point. Now noting that that correlation length $\zeta \sim \ln((T - T_c)/T_c)$ diverges as $T \to T_c$ and setting $\zeta \sim 2\pi / 4q$ for the long wavelength modes, we find $\kappa_\nu(q) \propto \lambda q^2 \ln q$ in the long wavelength limit, in agreement with our one-loop result above.

In the above, although we have neglected $\lambda_2$ and $\lambda$, the effective coupling $\lambda_2 = \lambda\lambda_2$ becomes marginal at $D = 4$, and hence should be equally relevant as $\mu$ and $\lambda$ in a DRG sense. Indeed, there are additional one-loop corrections to the various bare model parameters that originate from $\lambda_2$ (not shown here). Nonetheless, as our one-loop effective free energy $F_{\nu}$ suggests, the critical behaviour of $\phi$-fluctuations should still belong to the 2D Ising universality class. Thus, proceeding as above the divergence of $\kappa_\nu(q)$ near $T_c$ remains unchanged.
Appendix E. Fluctuation induced shift in $T_c$

We now heuristically argue in favour of experimental accessibility of second order MPT and first order MPT in the system. Apart from the well-known shift in $T_c$ due to the $u$-term in equation (9) \cite{9}, there is a correction to $T_c$ of the form $\lambda_1 \langle \nabla^2 \phi \rangle$, which is obviously finite. Additionally, a nonzero $\lambda_\nu$ should lead to a fluctuation-induced shift in $T_c$. The corresponding one-loop Feynman diagram is shown in figure E1 below. The expression is of the form $\sim \lambda_\nu D_h h \frac{d}{d(2\nu)} \frac{d}{d(2\nu-2)}$, which is finite. Thus, the shift in the mean-field $T_c$ due to the active effects is finite. This leads us to speculate that renormalised $T_{cR}$, i.e. the shifted or fluctuation-corrected $T_c$ should fall in a temperature range similar to the equilibrium critical points of model lipid bilayers, and correspondingly, any putative second order MPT should be accessible in experiments, at least for certain choices of the parameters of the model system. Furthermore, if we construct an effective Landau MF in terms of $u$, and $T_{cR}$, the first order transition temperature $T^*$ also gets a shift. Since $T_{cR}$ is expected to be experimentally accessible, the shifted $T^*$ should also be accessible experimentally for certain choices of the parameters of the model system. Thus, we speculate that it should be possible to observe MPTs (first order MPT or second order MPT) in certain inversion-symmetric lipid membranes, with properly tuned values of the model parameters, within experimentally accessible temperature ranges.

Appendix F. Composition-dependent surface tension

We now briefly consider the effects of a composition-dependent surface tension $\sigma(\phi)$. For simplicity we choose $\sigma(\phi) = \lambda_3 \phi^2 + \lambda_4 \phi$ in the free energy $\mathcal{F}$ as given in (6). For reasons of thermodynamic stability, we choose $\lambda_3 > 0$; the sign of $\lambda_4$ is arbitrary and may be absorbed in the definition of $\phi$. We choose the magnitude of $\lambda_4$ in a way to ensure $\sigma(\phi) > 0$ for all $\phi$, again to ensure thermodynamic stability. This now yields

$$\frac{\partial h}{\partial t} = \Gamma_h \big[ (\lambda_3 \phi^2 + \lambda_4 \phi) \nabla^2 h - \kappa \nabla^4 h + \lambda_4 \nabla \cdot (\phi \nabla h) \\ + \lambda_4 \nabla \cdot (\phi \nabla h) \big],$$

$$\frac{\partial \phi}{\partial t} = \Gamma_\phi \nabla^2 \left[ r \phi - \nabla^2 \phi + \frac{\mu}{3!} \phi^3 + 2 \lambda_3 \phi (\nabla^2 h)^2 + g \phi^2 \\ + \lambda_2 (\nabla^2 h)^2 + \nu \phi^5 + (2 \lambda_3 \phi + \lambda_4) \nabla^2 h \\ + \nabla \cdot f_\phi \right].$$  \hspace{1cm} (F1)

Thus, compared to equation (8), there are additional terms with coefficients $\lambda_3$, $\lambda_4$ in equation (F1). Notice also that the term $\lambda_4 \nabla \cdot (\phi \nabla h)$ has the same number of $\phi$ and $h$ fields as in the active $\lambda$-term in equations (8) or (F1); similarly, the term $\lambda_4 \nabla \cdot (\phi \nabla h)$ has the same number of $\phi$ and $h$ fields as in the active $\lambda$-term in equations (8) or (F1). Still, these $\lambda_3$- and $\lambda_4$-terms are total derivatives, where as the active $\lambda$ and $\lambda$-terms are not. Thus in the hydrodynamic limit, the $\lambda_3$- and $\lambda_4$-terms may be neglected (in a scaling sense) in comparison with the $\lambda$ and $\lambda$-terms in (F1). It is important to note that if $\sigma(\phi)$-term is included in $\mathcal{F}$, then the upper critical dimensions [9] of the $\lambda_3$- and $\lambda_4$-terms are 4 and 6, respectively. Thus, the MPT of the $\phi$-fluctuations should no longer belong to the 2D Ising universality in the equilibrium limit. Given that in our work, we have considered a tensionless membrane that undergoes only second order MPT with 2D Ising universality at equilibrium, we set $\sigma(\phi) = 0$ identically in our work.

Appendix G. Hydrodynamic friction and active stresses

We now consider the effects of hydrodynamic friction, hitherto ignored, on the dynamics of a tensionless mixed membrane. We include the effects of an active (nonequilibrium) stress $\sigma_{ij} = \gamma (\phi) P_{ij}$ (see, e.g. \cite{10}), that is generically present in an active fluid. (This $\phi$-dependent active stress again reflects specific lipid dependence of
the actin-lipid interactions.) With \( p_x = 1, p_j = \partial_j h, j = x, y, \) this makes a contribution of the form 
\( \partial_i (\gamma(\phi) p_j p_j) \) to \( v_{\text{hydro}} \) at \( z = h \); see [12]. We now choose \( \gamma(\phi) = A \phi^2 + B \phi. \) Because of their active origins, there are no restrictions on the magnitudes and signs of \( A \) and \( B. \) If hydrodynamically damping is considered, equation (8) in the presence of the active stresses, modifies to (with the choice \( X(\phi) = \Gamma_h(\lambda \phi^2 + \lambda \phi) \), see above)

\[
\frac{\partial h}{\partial t} = -\mu_p \frac{\delta F}{\delta h} + \Gamma_h[\lambda \phi^2 \nabla^2 h + \lambda \phi \nabla^2 h] + \Gamma'_h \left[ \frac{\delta F}{\delta h} + A \nabla \cdot (\phi^2 \nabla h) + B \nabla \cdot (\phi \nabla h) \right] + f_h, \tag{G1}
\]

where \( \Gamma'_h \) is a damping coefficient. The terms within square brackets in (G1) with coefficients \( \Gamma'_h \) come from the solution of the 3D hydrodynamic velocity field \( v_{\text{hydro}} \) [12]:

\[
v_{\text{hydro}} = \Gamma'_h \left[ \frac{\delta F}{\delta h} + A \nabla \cdot (\phi^2 \nabla h) + B \nabla \cdot (\phi \nabla h) \right]. \tag{G2}
\]

For a constant \( \Gamma'_h \), active terms with coefficients \( A \) and \( B \) in (G2) are total derivatives, and hence are subdominant (in a scaling sense) to those with coefficients \( \lambda, \lambda' \) in the hydrodynamic limit. Then, neglecting these \( A \)- and \( B \)-terms, we obtain equation (8) above. For hydrodynamic friction, \( \Gamma'_h = 1/(4\eta q) \) in the Fourier space, where \( \eta \) is the ambient fluid viscosity (see [21, 22]). As a result the \( A \)- and \( B \)-terms no longer vanish in the hydrodynamic limit \( q \rightarrow 0 \), and hence compete with the active terms with coefficients \( \lambda, \lambda' \). Then, with \( \Gamma'_h = 1/(4\eta q) \), the \( A \)- and \( B \)-terms contain fewer derivatives than the \( \lambda \)- and \( \lambda' \)-terms, respectively. This may be shown in a formal way. Replace \( \phi^2 \) by \( \langle \phi^2 \rangle \) and \( \phi \) by \( \langle \phi \rangle = 0 \) in the rhs of (G1) above in a mean-field like approximation. This allows us to extract two active tensions:

\[
s_a^h = A \langle \phi^2 \rangle, \quad s_a = \lambda \langle \phi^2 \rangle. \tag{G3}
\]

The former is the active hydrodynamic tension, where as the latter one is the active nonhydrodynamic tension [see equation (15)]. Equivalently, comparing with a tensionless isolated fluid membrane, we define an effective hydrodynamic bending modulus \( \kappa^h = \kappa + A \langle \phi^2 \rangle / q^2 \), in analogy with equation (17). In the long wavelength limit, in terms of ignoring the nonlinear terms, the effective dynamics of \( h \) in the Fourier space is given by

\[
\frac{\partial h(q, t)}{\partial t} = \left[ \mu_p \kappa_e(q) q^4 + \frac{\kappa^h}{4 \eta} q^4 \right] h(q, t) + f'_h, \tag{G4}
\]

The zero-mean, Gaussian white noise \( f'_h \) should have a variance given by

\[
\langle |f'_h(q, \omega)|^2 \rangle = 2D_h + 2D'_h/q, \tag{G5}
\]

\( D'_h > 0 \). Equation (G4) then yields for the equal-time membrane height correlator

\[
\langle |h(q, t)|^2 \rangle = \frac{D_h + D'_h/q}{\mu_p \kappa_c q^4 + \kappa^h q^4/(4 \eta)}. \tag{G6}
\]

The active coefficients \( \lambda \) and \( A \) are formally independent of each other and can be positive or negative separately. As a result, a variety of situation may emerge. (i) If \( \lambda \) and \( A \) have the same sign—both positive or both negative, we may neglect the \( A \)-term in comparison with the \( A \)-term, and \( \Gamma_h \kappa^h \) in comparison with \( \kappa^q q^2/(4 \eta) \) in (G6). Thus the long wavelength fluctuations of \( h(q, t) \) is now controlled by \( \kappa^h. \) Since \( A \) can be positive or negative (just like \( \lambda \)), \( \kappa^h \) varies with \( A \) yielding an \( L \)-dependence similar to that for \( \kappa_c \) in the main text. This evidently yields similar scaling behaviours for \( \Delta_\perp \) and \( \Delta_h \) (as defined in the main text) across first order MPT and second order MPT, with now \( A \) playing the role of \( \lambda \) in the main text. Thus, the correspondence between MPTs and the membrane conformation fluctuations that is elucidated above with just nonhydrodynamic friction, survives with hydrodynamic friction as well. Furthermore, for an impermeable membrane (for which \( \gamma_{\text{perm}} = 0 \), i.e. \( \lambda = 0 = \lambda' \)) with hydrodynamic friction, \( \Delta_\perp \) and \( \Delta_h \) behave the same way as above across second order MPT and first order MPT, again establishing the direct correspondence between membrane conformation fluctuations and MPT, now for an impermeable membrane. (ii) Different signs of \( A \) and \( \lambda \) in this case, one would encounter instabilities. For instance, with \( A < 0 \) and \( \lambda > 0 \), the model displays instabilities at the smallest wavevectors, where for the opposite case \( A > 0, \lambda < 0 \), the system remains stable at the smallest wavevectors, but shows finite wavevector instabilities controlled by the relative magnitudes of \( A \) and \( \lambda \). To what degree \( A \) and \( \lambda \) can be independently controlled and the biological significance of these results can be studied numerically by using properly constructed atomistic models.
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