Fluctuations of Quasi-Two-Dimensional Smectics Intercalated between Membranes in Multilamellar Phases of DNA-Cationic Lipid Complexes

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(Received 1 December 1997)

We theoretically elucidate lamellar phases of DNA-cationic lipid complexes as the very first realization of a *decoupled* phase of strongly fluctuating 2D smectic DNA manifolds weakly interacting across membranes. Because of couplings between adjacent 2D smectic $L_x \times L_y$ planes, recently observed ordinary 2D smectic behavior of DNA in-plane undulations, with $\langle u^2 \rangle \sim L_y^{1/2} \sim L_x$, must cross over, at long scales, to a novel fluctuation behavior, with $\langle u^2 \rangle \sim (\ln L_y)^2 \sim (\ln L_x)^2$. [S0031-9007(98)06039-6]

PACS numbers: 87.22.Bt, 05.40.+j, 61.30.Eb, 82.70.Kj

Soft condensed matter systems such as liquid crystals exhibit a variety of striking effects induced by thermal fluctuations. A classical example is the well-known Landau-Peierls divergence of smectic-A displacement fluctuations which destroys true long-range order in these phases. For the smectic layer displacement u, Landau and Peierls found, for *three-dimensional* smectics-A, $\langle u^2 \rangle \sim \ln(L)$, where L is the size of the smectic sample [1]. Thermal fluctuation effects are even more pronounced in experimentally rare *two-dimensional* smectics. There, smectic layers are *lines* fluctuating in a plane (e.g., long flexible molecules adsorbed on a smooth surface). For a sample of 2D smectic liquid crystal in the x-y plane (with layers perpendicular to the y axis), with sizes L_x and L_y, Toner and Nelson [2] found

$$\langle u^2 \rangle \sim L_x ,$$

for $L_x \ll \text{const} \times L_y^{1/2}$, whereas

$$\langle u^2 \rangle \sim L_y^{1/2}, \tag{1}$$

for $L_x \gg \text{const} \times L_y^{1/2}$. To date, the interest in 2D smectics was mostly theoretical [3]. Experimental interest in 2D smectics has revived in very recent works [4,5] on DNA-cationic lipid complexes which are able to carry (transfect) DNA across cell membranes for gene therapy applications. These complexes comprise interacting tensionless 1D DNA chains confined between 2D fluid membranes forming a lamellar, 3D smecticlike phase [4,5]. Intercalated DNA strands form a striking first example of strongly fluctuation *quasi-2D-smectic phases* only weakly interacting across lipid membranes, Fig. 1. Experimentally [5], these stacked quasi-2D smectic phases have only a short-range positional order due to divergent fluctuations of DNA in-plane displacements similar to undulations of true 2D smectics in Eq. (1). Here we study fluctuations in these novel phases that combine in *one*, many aspects of 2D smectics (short-ranged in-plane positional order due to strong long length scale undulations of DNA in the x-y planes) and of the conventional 3D smectics (thermal undulations along the z direction giving rise to the experimentally observed Landau-Peierls peaks). We theoretically elucidate this novel state of matter as the very first experimental realization of the so-called *decoupled* (unregistered) phase of strongly fluctuating 2D smectic manifolds weakly interacting across lipid membranes [6].

We address this phase of weakly interacting 2D smectic layers as a genuine 3D condensed matter system. Its elastic degrees of freedom involve the standard "in the x-y plane" undulations of 2D smectic layers (DNA molecules), $u(x, y, z)$, along the y direction, and, also, out-of-plane displacements along the z direction, $h(x, y, z)$, corresponding to 3D smectic undulations; see Fig. 1. The decoupled phase elastic free energy density associated with these displacements is

$$E_{\text{dec}}(u, h) = E_{\text{com}}(u, h) + E_{\text{bend}}(u, h) . \tag{2}$$

Here E_{com} is compressional energy density of the form

$$E_{\text{com}}(u, h) = \frac{B_{\text{sm}}^{(2D)}}{2}\left(\frac{\partial u}{\partial y}\right)^2 + \overline{B}\frac{\partial u}{\partial y}\frac{\partial h}{\partial z} + \frac{B_{\text{sm}}^{(3D)}}{2}\left(\frac{\partial h}{\partial z}\right)^2 \tag{3}$$

within harmonic approximation. E_{bend} in (2) is of the form

$$E_{\text{bend}} = E_{\text{bend}}^{(3D)} + E_{\text{bend}}^{(2D)} + E_{\text{bend}}^{\text{int}} , \tag{4}$$

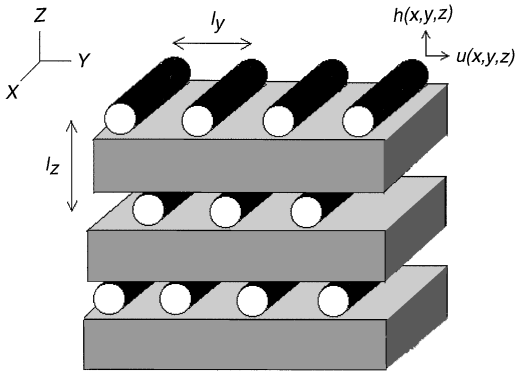

FIG. 1. Sketch of DNA/lipid membrane complex with DNA intercalated between membranes. Elastic degrees of freedom are the in-plane undulations $u(x, y, z)$ along the y axis, and out-of-plane undulations $h(x, y, z)$ along the z axis. DNA chains (black) are, on average, along the x axis.

where $E_{\rm bend}^{(3D)}$ includes 3D smectic bending terms due to the membrane curvature elasticity energy anisotropically (biaxially) modified due to the presence of DNA chains oriented along the x axis,

$$E_{\rm bend}^{(3D)} = \frac{K_{yy}^{(3D)}}{2}(\partial_y^2 h)^2 + \frac{K_{yx}^{(3D)}}{2}(\partial_y\partial_x h)^2 + \frac{K_{xx}^{(3D)}}{2}(\partial_x^2 h)^2. \quad (5)$$

$E_{\rm bend}^{(2D)}$ in (4) is the ordinary 2D smectic bending term, $\frac{1}{2}K_{\rm sm}^{(2D)}(\partial_x^2 u)^2$. Finally, $E_{\rm bend}^{\rm int}$ in (4) is an elastic energy density cost of the form

$$E_{\rm bend}^{\rm int} = \frac{K_{zx}}{2}\left(\frac{\partial^2 u}{\partial z\partial x}\right)^2 + \frac{K_{zy}}{2}\left(\frac{\partial^2 u}{\partial z\partial y}\right)^2. \quad (6)$$

Physically, the K_{zx} term in (6) corresponds to the coupling of local 2D-smectic tilts ($= \partial_x u$) between neighboring 2D smectics. Likewise, the K_{zy} term in (6) describes the coupling of local 2D smectic layer densities ($= \partial_y u$) between neighboring 2D smectics. These two terms, as well as the $\overline{B}$ term in (3), are the major (most relevant) terms describing interactions *between* neighboring 2D smectics in this "decoupled" phase of matter. On the other side, macroscopic shear coupling between neighboring 2D smectics, of the form

$$\frac{\mu}{2}\left(\frac{\partial u}{\partial z} + \frac{\partial h}{\partial y}\right)^2, \quad (7)$$

is *forbidden* in the long length scale elastic energy of *decoupled* phases. Such a term, though, would appear in the elastic energy of a *columnar* phase which may also occur in these systems. The presence of a nonzero *macroscopic* shear modulus μ stabilizes long-range positional order. This is in clear contradiction to the experimental observations on DNA-cationic lipid lamellar phases [4,5], supporting our realization that DNA-cationic lipid lamellar phase is, in fact, a decoupled phase. The absence of the macroscopic shear modulus is related to a striking *local* (gauge) translational invariance of the decoupled phase of the form

$$u(x, y, z) \to u(x, y, z) + f(z), \quad (8)$$

where $f(z)$ is an *arbitrary* function of z [7]. This local symmetry reflects the fact that, in the decoupled (unregistered) phase, 2D smectics can be continuously *individually* ("locally") translated (slid) along the y direction with no free energy costs. This local symmetry prohibits not only the shear energy cost (7) in the compressional energy (3) but also energy density costs of the form

$$\frac{K_{zz}}{2}\left(\frac{\partial^2 u}{\partial z^2}\right)^2, \quad (9)$$

which one may naively include along with other similar terms in Eq. (6). The absence of this term is crucial for an uncommon fluctuation behavior we find in the following. Its appearance is best seen by considering the effective elastic free energy obtained by integrating out-of-plane undulations $h(x, y, z)$ out of the partition function of $E_{\rm dec}(u, h)$. This yields the effective free energy density for the in-plane undulations $u(x, y, z)$ of the form

$$E_{\rm eff}(u) = \frac{\tilde{B}_{\rm sm}^{(2D)}}{2}\left(\frac{\partial u}{\partial y}\right)^2 + \frac{K_{\rm sm}^{(2D)}}{2}\left(\frac{\partial^2 u}{\partial x^2}\right)^2 + \frac{K_{zx}}{2}\left(\frac{\partial^2 u}{\partial z\partial x}\right)^2 + \frac{K_{zy}}{2}\left(\frac{\partial^2 u}{\partial z\partial y}\right)^2, \quad (10)$$

plus irrelevant terms. Here, $\tilde{B}_{\rm sm}^{(2D)} = B_{\rm sm}^{(2D)} - \overline{B}^2/B_{\rm sm}^{(3D)}$. By (10) and the equipartition theorem, we obtain

$$\langle |u(\mathbf{q})|^2\rangle = \frac{k_B T}{\tilde{B}_{\rm sm}^{(2D)} q_y^2 + K_{\rm sm}^{(2D)} q_x^4 + q_z^2(K_{zx}q_x^2 + K_{zy}q_y^2)}, \quad (11)$$

for the correlation function in q space. A notable feature of the correlations in (11) is that they diverge along an entire *line* in the q space, namely, along the q_z axis ($q_y = q_x = 0$). The emergence of such a "*soft axis*" is in marked contrast to more common ordered liquid crystalline phases, such as smectics [1], for which fluctuations diverge only at a *soft point* in q space, $q_x = q_y = q_z = 0$. This unusual feature of decoupled phases is directly caused by their gauge symmetry (8) prohibiting elastic energy costs such as (7) and (9) which would contribute the terms μq_z^2 and $K_{zz}q_z^4$ to the denominator of (11). In their absence, fluctuations diverge along the *entire* q_z axis rather than just at $\mathbf{q} = 0$.

In DNA-cationic lipid complexes, the presence of the soft axis gives rise to an unusual fluctuation behavior discussed hereafter. Experimentally [5], these stacked quasi-2D smectic phases exhibit only a short-range in-plane positional order due to divergent fluctuations of DNA in-plane displacements $u(x, y, z)$ similar to those of true 2D smectics in Eq. (1). Such a true 2D behavior would correspond to the limit of vanishing interplane coupling constants K_{zx} and K_{zy} in Eqs. (10) and (11). By (11), we find that these couplings between neighboring 2D smectics do not restore DNA positional order, as DNA thermal in-plane undulations $\langle u^2\rangle = \int_q \langle |u(q)|^2\rangle$ still diverge with increasing sizes L_x and L_y of the 2D smectic planes. However, the interplane couplings turn out to qualitatively affect the physics at long scales. So, the experimentally observed behavior [5], with $\langle u^2\rangle \sim L_y^{1/2} \sim L_x$ [as in true 2D smectics [2], Eq. (1)] occurs only at short enough scales. At long enough scales, the interplane couplings K_{zx} and K_{zy} dominate. There we predict, by applying our Eq. (11), an unusual, more isotropic fluctuation behavior, in which $\langle u^2\rangle$ grows as the *square of the logarithm* of the system sizes,

$$\langle u^2\rangle \sim (\ln L_x)^2, \quad (12a)$$

for $L_x \ll L_y$, and

$$\langle u^2\rangle \sim (\ln L_y)^2, \quad (12b)$$

for $L_y \ll L_x$. On the other hand, fluctuations of the ordinary (out-of-plane) 3D-smectic-like undulations, $\langle h^2 \rangle$, grow just as the *first* power of the logarithm of the system size, i.e., in the standard Landau-Peierls fashion. Experimentally measured correlations of the in-plane modulated density $\rho(x,y,z) \sim \mathrm{Re}\ \exp\{i\frac{2\pi}{l_y}[y - u(x,y,z)]\}$ [obtained from the "DNA peak" [5] of $\langle|\rho(\mathbf{q})|^2\rangle$ at $q_y = \frac{2\pi}{l_y}$, $q_x = q_z = 0$] must be short ranged due to the divergent behavior of in-plane undulations u in Eq. (12). Within the harmonic theory, $K(x,y,z) = \langle \rho(x,y,z)\rho(0,0,0)\rangle \sim \exp[-\frac{1}{2}(\frac{2\pi}{l_y})^2 C(x,y,z)]$, with

$$C(\mathbf{r}) = \langle [u(x,y,z) - u(0,0,0)]^2 \rangle = 2\int \frac{d^3q}{(2\pi)^3} \langle |u(\mathbf{q})|^2 \rangle [1 - \exp(i\mathbf{qr})],$$

and $\langle |u(\mathbf{q})|^2 \rangle$ as in (11). For the *in-plane* correlations ($z = 0$) we thus predict, in accord with Eq. (12),

$$K(x,y,z=0) \sim \exp\left[-\eta\left(\ln\frac{x}{x_*}\right)^2\right], \tag{13a}$$

for $x/y \gg (K_{zx}/K_{zy})^{1/2}$, and $x \gg x_{\min} = l_z(K_{\mathrm{sm}}^{(2\mathrm{D})}/K_{zx})^{1/2}$, whereas

$$K(x,y,z=0) \sim \exp\left[-\frac{\eta}{2}\left(\ln\frac{y}{y_*}\right)^2\right], \tag{13b}$$

for $x/y \ll (K_{zx}/K_{zy})^{1/2}$, and $y \gg y_{\min} = x_{\min}^2/\lambda$, with $\lambda = (K_{\mathrm{sm}}^{(2\mathrm{D})}/\tilde{B}_{\mathrm{sm}}^{(2\mathrm{D})})^{1/2}$. In Eq. (13), $\eta = k_BT/l_y^2(K_{zx}\tilde{B}_{\mathrm{sm}}^{(2\mathrm{D})})^{1/2}$, $x_* \sim \lambda(K_{zx}/K_{zy})^{1/2}$, and $y_* \sim x_*^2/\lambda$. Correlations in Eqs. (13a) and (13b) are the most significant result of this Letter. They have an uncommon power-law-like decay, with *scale dependent* exponents changing slowly as logarithm of the length scale. For example, by (13a), $K(x, y=0, z=0) \sim x^{-\eta(x)}$, with $\eta(x) = \eta\ln(x) + \mathrm{const}$. This novel behavior occurs for $x \gg x_{\min}$ or $y \gg y_{\min}$, at scales shorter than a (large) topological defect length scale ξ_{def} discussed in the following. On the other side, at length scales shorter than $(x_{\min}, y_{\min})$, we find the ordinary 2D smectic correlations [2] already observed in Ref. [5]. Another experimentally interesting issue is the modulated density correlations between *different* 2D smectic planes in the stack, $K(x,y,z \neq 0)$. Within the continuum elastic theory, we find *vanishing* $K(x,y,z \neq 0)$. This is related to a bizarre divergence of *relative* in-plane displacements between the *nearest-neighbor* 2D smectics, induced by the presence of the soft axis in (11),

$$\langle [u(x,y,z+l_z) - u(x,y,z)]^2 \rangle \sim \ln(L_x) \sim \ln(L_y). \tag{14}$$

So, $C(x=0, y=0, z=l_z) = \infty$, and, thus, $K(x=0, y=0, z=l_z) = 0$ in thermodynamic limit. However, the presence of the interplane modulated density correlations has been evidenced in recent experiments [5]. Here we rationalize these correlations as an effect of a *microscopic* sine-Gordon (SG) shear coupling, of the form

$$E_{\mathrm{SG}} = -A\cos\left(\frac{2\pi}{l_y} D_z u\right). \tag{15}$$

Here $D_z u = u(x,y,z+l_z) - u(x,y,z) + l_z\partial_y h$; as in Fig. 1, l_z is the equilibrium distance between 2D-smectic planes (at $z = nl_z$), whereas l_y is the 2D smectic repeat distance. This coupling is irrelevant at *long* scales, due to divergence in Eq. (14). Thus, 2D smectics see their neighbors as smooth anisotropic 2D manifolds, and *macroscopic* shear modulus [μ in Eq. (7)] is zero. However, it would be wrong to ignore E_{SG} is one is interested, e.g., in *short*-range correlations of the in-plane modulated density $\rho(x,y,z) \sim \mathrm{Re}\ \exp\{i\frac{2\pi}{l_y}[y - u(x,y,z)]\}$ between *different* 2D smectic planes in the stack. Such short-range correlations generally *vanish* with vanishing strength A of the microscopic SG shear term in Eq. (15) [i.e., for $A \to 0$, the correlation function $K(x,y,z) = \langle \rho(x,y,z)\rho(0,0,0)\rangle$ vanishes for $z \neq 0$]. By perturbative (cumulant) expansion in powers of the shear coupling A in (15) we compute these interplane correlations [8]. For example, for the nearest-neighbor smectic planes, we find $K(x=0, y=0, z=\pm l_z) \sim A$, and for the next-nearest-neighbor planes, we find $K(x=0, y=0, z=\pm 2l_z) \sim A^2$, etc. Furthermore, though irrelevant, sine-Gordon shear coupling (15) renormalizes (stiffens) the elastic constants K_{zx} and K_{zy} [8]. To order A^2, this renormalization is of the form $\Delta K_{zx} \sim \int d^3r\, x^2 K_{\mathrm{SG}}(\mathbf{r})$, with $K_{\mathrm{SG}}(\mathbf{r}) = \langle E_{\mathrm{SG}}(0)E_{\mathrm{SG}}(\mathbf{r})\rangle_{E_{\mathrm{dec}}}$. By (11), we find $K_{\mathrm{SG}}(\mathbf{r}) \sim \delta(z)x^{-\omega} \sim \delta(z)y^{-\omega}$, with a nonuniversal exponent ω. For example, $\omega \approx \pi 2^{3/2}\eta$, for $\tilde{B}_{\mathrm{sm}}^{(2\mathrm{D})} \gg K_{zy}/l_y^2$; here $\eta \sim k_BT$ is the materials constant entering Eq. (13). As ΔK_{zx} must remain finite, it must be that $\omega > 4$ (i.e., $\eta > 2^{1/2}/\pi$) in the decoupled phase stability range. For $\omega < 4$, *arbitrarily* weak sine-Gordon shear coupling (15) is relevant and converts the decoupled phase into the columnar phase (with a nonzero shear modulus $\mu \sim A$). As $\omega \sim k_BT$, it is clear that the decoupled phase is *only* entropically favored over the columnar phase.

Topological defects, such as DNA hairpin turns, soften elastic constants of the decoupled phase. To the lowest order in hairpin turns fugacity $z_{\mathrm{hp}} = \exp[-E_{\mathrm{core}}/k_BT]$, this softening is $\sim -z_{\mathrm{hp}}^2 \int d^2r\, r^2 \exp[-U(r)/k_BT]$, with $U(r) = \omega_1 k_BT\ln(r)$ (the in-plain hairpin turn interaction potential), and $\omega_1 = 2/\omega$ for $\tilde{B}_{\mathrm{sm}}^{(2\mathrm{D})} \gg K_{zy}/l_y^2$ [8]. This softening is finite (i.e., the defects are irrelevant) only if $\omega_1 > 4$. However, as $\omega > 4$ in the decoupled phase stability range, one has $\omega_1 = 2/\omega < 1/2$ there. Thus, hairpin turns are *relevant* and turn the decoupled phase into a *nematiclike* phase (with *easy* x-y plane) at scales longer than the defect scale $\xi_{\mathrm{def}} \sim (z_{\mathrm{hp}})^{-2/(4-\omega_1)}$. For example, for $\omega_1 \ll 1$, $\xi_{\mathrm{def}} \sim (z_{\mathrm{hp}})^{-1/2} \sim \exp[E_{\mathrm{core}}/2k_BT]$. For the system of Ref. [5], we estimate $E_{\mathrm{core}}/k_BT \approx 30$ [8]. Thus, (i) ξ_{def} is huge there, and there is a broad range

of length scales for observing the defect-free correlations in Eq. (13); (ii) a more isotropic liquidlike state of DNA chains, produced by disordering the nematiclike phase orientationally within the easy x-y plane, seems unlikely to occur in *equilibrium* in the system of Ref. [5] (unless the interplane couplings can be made exceedingly small).

Thus far, for simplicity, we ignored chirality effects of DNA. They are presumably weak in the experimental realization [4,5]. Still, even a *weak* chirality may modify the structure of the decoupled phase in these systems: It contributes the terms of the form $-g_{\rm chiral}\partial_z\partial_x u$ to the elastic energy of the decoupled phase (10). This chiral term twists 2D smectic planes around the z axis and turns the decoupled phase into a "tilt-grain-boundary" (TGB) phase (like that discussed in [9]) with the "cholesteric" pitch period $\lambda_{\rm pitch} = 2\pi K_{zx}/g_{\rm chiral}$ along the z direction. This twist, however, does not qualitatively affect the form of the in-plane correlations. They are still as in Eq. (13) in a suitably twisted coordinate system, with x-y planes locally rotated around the z axis by the angle $= 2\pi z/\lambda_{\rm pitch} = z g_{\rm chiral}/K_{zx}$. Interestingly, *arbitrarily weak* $g_{\rm chiral}$ can transform the decoupled phase into a TGB phase, essentially because 2D smectics see their neighbors as smooth 2D manifolds. This peculiarity is in marked contrast to the behavior of the columnar phase which transforms into the TGB phase only if $g_{\rm chiral}$ exceeds a finite critical value [9].

We thank Tim Salditt for communicating to us Ref. [5] prior to its publication. This work was supported by a Mylan Laboratories, Inc., research grant.

Note added.—After submitting this Letter, we learned of a similar work of O'Hern and Lubensky [10].

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$$u(x,y,z) \to u\big(x, y + f(z), z\big) + f(z),$$
$$h(x,y,z) \to h\big(x, y + f(z), z\big),$$

where $f(z)$ is an arbitrary function of z (here we employed Lagrangian elasticity picture). This reduces, for small strains, $\partial_y u, \partial_y h \ll 1$, to the harmonic approximation gauge invariance in Eq. (8). On the other side, in a *columnar* phase, the above continuous local symmetry is broken down to discrete local symmetry for which local translation $f(z) = l_y m(z)$. Here $m(z)$ is an arbitrary integer valued function of z = multiple of l_z.
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