Elastic deformations of grafted layers with surface stress

A. Nicolas and S. A. Safran
Department of Materials and Interfaces, Weizmann Institute of Science, Rehovot 76100, Israel
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We calculate the elastic response of thin films grafted to a solid substrate whose upper surface is subject to a stress. This issue is addressed in the context of biological cell adhesion where adhesive junctions consist of a thin layer of proteins grafted to the extracellular matrix and sheared by the cell contractility apparatus. We show that the finite thickness of the layer limits stress-induced deformations to short ranges proportional to the thickness of the film. In addition, we show that the attachment boundary condition creates an effective shear response to surface stresses that couples all the directions, even for fluidlike layers. We predict that perturbations with wavelengths of order of the film thickness induce resonancelike responses for isotropic rubberlike materials or anisotropic media with high shear moduli. We use these results to predict the elastic deformations of a layer of proteins under shear stress and propose that the resulting, polarized elastic response to local surface forces can explain the observed, anisotropic growth of cell-substrate junctions when subject to external stresses.

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I. INTRODUCTION

The transmission of stress in cells attached to a surface is of crucial importance for the understanding of biological cell adhesion on either a substrate or in a three-dimensional matrix. Cell-matrix or cell-substrate adhesions (also called focal contacts) are clusters of proteins that are able to dynamically adjust both their size and shape to the applied stress [1–3] (see Fig. 1). While the adhesive force is normal to the substrate, the large-scale structure of focal contacts are strongly influenced by lateral shear forces that occur in cells due to the action of the elastic cytoskeleton on the protein clusters. These lateral forces induce an anisotropic aggregation of additional proteins and cause the aggregate to expand at the front edge of the stressed region; this effect is independent of the origin of the force (contractility of the cytoskeleton within the cell, external forces such as shear flow [4], or externally applied local forces [5]). The ability of the adhesive junctions to respond to such forces allows the cell to adapt its shape and function to the physical properties of the substrate [6]; for example, this effect is responsible for the migration of the cell to the most rigid regions of the substrate [7–9]. Although the biochemistry of focal contacts is beginning to be understood [10], the link between the mechanical perturbation and the anisotropic biochemical response of the contacts that causes the junctions to grow in the direction of the force is still a mystery. Here, we propose that the coupling of the mechanical and biochemical response has its origin in the elastic deformations of the layer of proteins that comprise the focal contact. When this layer is submitted to an internal or external directional stress, there is a resulting, *anisotropic* density change in the surrounding region that strongly affects the further aggregation of proteins to the focal contacts. We suggest that the physics presented here may explain the observed anisotropic growth of cell-substrate junctions that are subject to external stresses. The detailed consequences of this elastic response for cell adhesion will be discussed elsewhere [11].

The elastic response of thin films to surface stresses has important implications in the context of the theory of elasticity and its applications to grafted layers. Elastic deformations in bulk media give rise to long-range interactions [12]: a local stress applied to a *infinite* two-dimensional plate causes a deformation that depends logarithmically on the distance from the stress. However, this long-range response is strongly influenced by the boundary conditions [13]. For example, the range of deformation is limited to the film thickness in finite, elastic medium; the details depend on the various boundary conditions on both surfaces. Here, we consider a film that is composed of molecules tethered to the surface as a model of cell-substrate adhesions. We predict how elastic deformations are modified for such grafted layers whose top surface is submitted to a stress and that several effects arise as a result of the grafting boundary condition. The first effect is the creation of a boundary condition-induced, effective, shear response to surface forces that exists even for liquidlike layers such as amphiphilic or lipid monolayers. A second major effect arises from the finite thickness of the layer. Contrary to a semi-infinite elastic medium, the elastic interactions are now short range with the range of the interaction of the order of the thickness. We predict that rubberlike materials or anisotropic media with strong shear moduli can respond in a "resonancelike" manner to perturbations at certain wavelength determined by the film thickness and the elastic properties of the material. Finally, we show that a localized surface force results in an anisotropic, in-plane re-

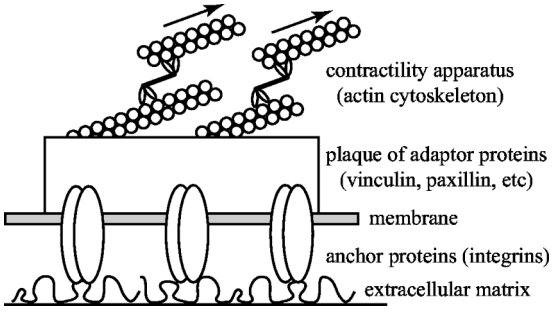

FIG. 1. Schematic representation of a focal contact.

sponse of the film, the anisotropy being similar to that of a semi-infinite elastic medium. Systems with certain elastic properties, such as a strong mechanical stiffness of the grafted molecules, can lead to a directional perturbation that is determined by the symmetry of the force. Such a directional response may explain why adsorbed proteins layers involved in cell-substrate adhesions grow in an anisotropic manner when subject to surface shear forces. Proteins outside the region where the force applies are stressed differently depending on their position relative to the stressed region: the local density is increased at the front edge while decreased at the rear. This variation of the local density may be a possible trigger for initiating localized biochemical reactions that affect the propensity of proteins to aggregate at the front or the back with different probabilities. This effect may be the physical origin of the observed anisotropic growth of focal contacts upon application of internal or external stresses.

The following section of the paper introduces the elasticity of thin films such as amphiphilic layers grafted to a surface. By integrating over the elastic response in the direction perpendicular to the film, we derive in Sec. III, the effective response of the film to surface perturbations. We first treat surface perturbations that vary in only one direction in the plane of the film. The deformations due to surface stresses that vary in two dimensions in the plane are treated in Sec. IV, where we focus on the effective, in-plane shear modulus induced by the boundary effects; an effective shear modulus is predicted even for originally fluid thin films or monolayers. We show that the anisotropy of grafted layers leads to a polarized response to local surface forces which we propose as a mechanism for the anisotropic growth of cell-substrate junctions.

II. ELASTICITY OF A GRAFTED LAYER

Amphiphilic molecules in water assemble into monolayers or thin films at water-air or water-oil interfaces. The structure is fluid and there is no energy cost for shear deformations of these thin films. The fluid layer is fully described by its elastic moduli of compression: λ_{xxxx}, λ_{yyyy}, and λ_{zzzz}. Anchoring the monolayer or thin film to a surface (whose normal is in the $\hat{z}$ direction) results in an energy cost for shear deformations in the x-z or y-z planes. This occurs even though there is no intrinsic, solidlike order and is related to the fact that the layer is not homogeneous in the $\hat{z}$ direction; the shear tilts the molecules and changes their surroundings: hydrophobic tails get closer to hydrophilic heads, leading to an increase of the energy. Two sets of elastic moduli come into play when such a grafted layer is sheared: λ_{xzxz} (or λ_{yzyz}) related to the torque-induced shear, and λ_{xxzz} (or λ_{yyzz}) related to the compression-induced shear. No elastic coupling exists between x and y when the layer is not anchored but fluid. Tethering the layer to the surface does not change this property and the layer still has a zero, in-plane, bulk shear modulus: $\lambda_{xxyy}=\lambda_{xyxy}=0$. However, because of the x-z and y-z shear modulus, fluid layers are inherently anisotropic.

We now write the elastic energy of such a grafted layer that is isotropic in the x-y plane (C_{4v} symmetry):

$$\mathcal{E}=\int dx\,dy\,dz\left[\frac{\lambda_{xxxx}}{2}\left(u_{xx}^2+u_{yy}^2\right)+\frac{\lambda_{zzzz}}{2}u_{zz}^2+\lambda_{xxzz}\left(u_{xx}+u_{yy}\right)u_{zz}+2\lambda_{xzxz}\left(u_{xz}^2+u_{yz}^2\right)\right]. \quad (1)$$

The elastic moduli include contributions from both energetic interactions and entropy; in particular, the constant λ_{zzzz} arises from the mechanical stiffness of the chain [14]. These coefficients differ from the elastic properties of the bulk because the entropy of stretched chains at an interface is lower than that of chains in the bulk solution [15]. The system has two shear moduli λ_{xzxz} and λ_{xxzz} that have opposite responses to external stresses. The shear modulus λ_{xzxz} accounts for the energy associated with the deformation due to the torque imposed by the shear force: high values of λ_{xzxz} give rise to a vertical compression of the layer at the front edge and an expansion at the rear edge of the stressed zone. In contrast, the shear modulus λ_{xxzz} is related to the compressibility of the layer: a displacement in the x direction induces an excess of material at the front and a depletion of material in the back. Typical materials are isotropic and their elastic properties are defined by their Young modulus E and the Poisson ratio ν. The relationship between the moduli λ_{ijkl} and the Young modulus E and the Poisson ratio ν is [12]

$$\lambda_{xxxx}=\lambda_{zzzz}=\lambda_{yyyy}=\frac{E}{1+\nu}\frac{1-\nu}{1-2\nu},$$

$$\lambda_{xzxz}=\lambda_{yzyz}=\lambda_{xyxy}=\frac{E}{2(1+\nu)},$$

$$\lambda_{xxzz}=\lambda_{yyzz}=\lambda_{xxyy}=\frac{E}{1+\nu}\frac{\nu}{1-2\nu}. \quad (2)$$

The Poisson ratio ν usually ranges from 0.25 to 0.5. A Poisson ratio of 0.25 implies that $\lambda_{xzxz}=\lambda_{xxzz}$. For values of the Poisson ratio $\nu>0.25$, $\lambda_{xxzz}>\lambda_{xzxz}$ and the shear induces an excess of material (bump) at the edge of the stressed zone as we expect from intuition. Some materials with special properties such as foams or fixed-connectivity membranes [16,17] have negative Poisson ratios and therefore show atypical response to shear such as a vertical compression in front of the stressed zone and a bump at the rear.

III. DEFORMATION OF A GRAFTED FILM UNDER SHEAR FORCE

An initially fluid layer grafted onto a surface responds to small perturbations like an anisotropic elastic medium with the elastic energy Eq. (1). We consider the important case where the layer is grafted to the substrate on the bottom plane (at $z=0$) and subject to a localize stress that acts on the top plane (at $z=h$). We focus on the deformations on the surface (at $z=h$). The gradients of these deformations are proportional to the local surface density of the grafted molecules on the top of the layer. As detailed later on, the variation of the local density may be the relevant parameter that determines the anisotropic aggregation of additional proteins

in cell adhesion, leading to the growth of the focal contacts in the direction of the applied force.

The deformation of a grafted layer cannot be understood with the usual methods developed for two-dimensional films [13]. The boundary conditions that apply in the z direction are crucial to the determination of the elastic response of the film, even to surface stresses, and the three-dimensional nature of the finite layer must be considered. We now derive the Green's function for the response of such a layer. Most of the interesting aspects of this problem can be understood by focusingon a system where there are no variations of the grafting conditions nor the applied surface stresses in the y direction. It is this case, with variations of the deformations in only the thickness (z direction) and one surface direction (the x direction), that is treated in this section. In Sec. IV we treat the full problem with variations in both the x and y directions and show that the grafted layer exhibits a novel response to in-plane x-y shear deformations. However, for the sake of simplicity, we first focus on the case where there are variations only in x and z.

We first demonstrate that the grafting condition strongly modifies the usual long-range elastic interaction observed for semi-infinite media [12] and introduces a finite cutoff related to the film thickness and the elastic constants. We also point out the unusual nature of the elastic energy for thin films and explain the presence of terms that are independent of and linear in the wave vector of the deformation q (in addition to terms that are quadratic in q as in the bulk). We finally discuss the fact that large shear moduli can destabilize the layer and gives rise to an unusually large response of the film to perturbations with certain wavelengths determined by the elastic properties of the material (resonancelike behavior).

The two-dimensional layer is grafted to the substrate at $z=0$ and the top surface of the layer is at $z=h$. The elastic energy for a system invariant in y is

$$\mathcal{E}=\int dxdz\left[\frac{\lambda_{xxxx}}{2}u_{xx}^2+\frac{\lambda_{zzzz}}{2}u_{zz}^2+\lambda_{xxzz}u_{xx}u_{zz}+2\lambda_{xzxz}u_{xz}^2\right], \tag{3}$$

where the integral over z is from $z=0$ to $z=h$ and the integral over x extends to plus/minus infinity since we discuss layers whose lateral extent is much larger than the range or size of the surface stresses applied to the layer. This simple approach does not take into account the intrinsic anisotropy of an originally fluid layer since we focus on deformations that are invariant in the y direction. A gel and a grafted layer where tethered molecules are not entangled behave similarly under such deformations, but have of course different values for their elastic coefficients that correspond to the different entropic response of each systems [18]. The limit of an isotropic elastic medium can be obtained in Eq. (3) by replacing the elastic coefficients λ_{ijkl} by their relationship (2) with the Young modulus E and the Poisson ratio ν. Results obtained in this section are therefore completely general and are independent of the elastic anisotropy of the film. The spatial dependence of the deformation of the layer is given by minimizing the energy (3) subject to the boundary conditions

$$\vec{u}(x,0)=\vec{0},$$

$$\vec{u}(x,h)=\vec{u}_h(x).$$

One thus obtains the deformation as a function of both x and z. The elastic energy is obtained by substituting the deformation that minimizes the energy into Eq. (3). However, to focus on the effects of surface stresses, it is very useful to express the energy in terms of the surface displacement $\vec{u}_h(x)$ only. To this end, we integrate the energy over z. The results are best expressed in terms of the Fourier components of the surface strains $u_{qk}^h=u_{qk}(h)$, defined by the Fourier transform

$$u_k(x,z)=\frac{1}{\sqrt{2\pi}}\int u_{qk}(z)e^{iqx}dq.$$

Biologically relevant stresses have ranges of the order of fractions of microns, much larger than the thickness of the film which is typically in the nanometer range. We therefore focus on the case of long-wavelength deformations and expand the energy tosecond order in the dimensionless, small parameter that is the product of the wave vector q and the thickness h and we obtain

$$\mathcal{E}=\int\frac{dq}{2\sqrt{2\pi}}\left[\left(\frac{\tilde{\lambda}_x}{h}+\tilde{\lambda}_x'\,q^2h\right)|u_{qx}^h|^2+\left(\frac{\tilde{\lambda}_z}{h}+\tilde{\lambda}_z'\,q^2h\right)|u_{qz}^h|^2+\tilde{\lambda}_{xz}\,iq\,(u_{qx}^h\overline{u}_{qz}^h-\overline{u}_{qx}^h u_{qz}^h)\right]. \tag{4}$$

In this expression, $\overline{u}_{qk}^h$ is the complex conjugate of the complex quantity u_{qk}^h and $\tilde{\lambda}_{ij}$ are the effective elastic coefficients that result from the integration over the thickness:

$$\tilde{\lambda}_x=\lambda_{xzxz},\quad \tilde{\lambda}_x'=\frac{4\lambda_{xxxx}\lambda_{zzzz}-(\lambda_{xzxz}+\lambda_{xxzz})^2}{12\lambda_{zzzz}}, \tag{5}$$

$$\tilde{\lambda}_z=\lambda_{zzzz},\quad \tilde{\lambda}_z'=\frac{(\lambda_{xzxz}-\lambda_{xxzz})(3\lambda_{xzxz}+\lambda_{xxzz})}{12\lambda_{xzxz}}, \tag{6}$$

$$\tilde{\lambda}_{xz}=\frac{\lambda_{xxzz}-\lambda_{xzxz}}{2}. \tag{7}$$

Due to the grafting condition, the energy (4) includes a term that is independent of the wave vector q. This is because the finite film breaks the translational symmetry; shifting the top of the layer *does* cost energy and is similar to a shear deformation, as confirmed by the value of $\tilde{\lambda}_x$ (5). Another important effect is the existence of a term proportional to $\tilde{\lambda}_{xz}$ that is linear in the wave vector q. This term arises from the finite distance (proportional to $1/q$) that a surface perturbation penetrates into the material. Thus, although elastic energies usually depend quadratically on q, the effective thickness of the deformation region is proportional to $1/q$; integration of the elastic energy q^2 over the thickness repack $1/q$ results in an effective surface elasticity that has a term linear in q. Equation (7) also highlights the competition between the two kinds of shear moduli previously discussed;

the overall sign of the effective shear modulus $\tilde{\lambda}_{xz}$ depends on the relative contributions of each term.

When a force $\vec{f}(x)$ is applied on the top surface of the layer at $z=h$, the elastic energy is augmented by a term

$$-\int \vec{f}(x)\vec{u}(x,h)dx = -\int \frac{dq}{2\sqrt{2\pi}}(\vec{\bar{f}}_q\vec{u}_q^h + \vec{f}_q\vec{\bar{u}}_q^h). \quad (8)$$

The resulting deformation of the surface of the thin film is related to the external stress by the Green's tensor $G(x)$:

$$u_i(x,h) = \frac{1}{\sqrt{2\pi}}\int f_j(x')G_{ij}(x-x')dx'. \quad (9)$$

In Fourier space, within the approximation $qh \ll 1$, the Green's tensor is written

$$G_q \simeq \frac{h}{1+q^2\ell^2}\begin{pmatrix} \frac{1}{\tilde{\lambda}_x} & \frac{\tilde{\lambda}_{xz}}{\tilde{\lambda}_x\tilde{\lambda}_z}iqh \\ -\frac{\tilde{\lambda}_{xz}}{\tilde{\lambda}_x\tilde{\lambda}_z}iqh & \frac{1}{\tilde{\lambda}_z} \end{pmatrix}. \quad (10)$$

In two dimensions, the response of the thin film to a highly localized, delta function surface force is an exponential decay with a range ℓ that is determined by the elastic properties of the material:

$$\ell = h\sqrt{\frac{\tilde{\lambda}_x\tilde{\lambda}_z' + \tilde{\lambda}_x'\tilde{\lambda}_z - \tilde{\lambda}_{xz}^2}{\tilde{\lambda}_x\tilde{\lambda}_z}}$$

$$= h\sqrt{\frac{4\lambda_{xxxx}\lambda_{zzzz} - (5\lambda_{xxzz}^2 - 2\lambda_{xxzz}\lambda_{xzxz} + \lambda_{xzxz}^2)}{12\lambda_{xzxz}\lambda_{zzzz}}}. \quad (11)$$

We note that the range is only meaningful when $\ell^2 > 0$; however, this quantity can become negative since the term in parentheses in Eq. (11) is always positive. When the range ℓ becomes imaginary, this indicates that there is a destabilization of the smooth exponential decay. This may signify the appearance of oscillatory behavior or in some cases, long-range order. The response of the system is related to the amplitude of thermal fluctuations that diverges when ℓ^2 becomes negative:

$$\langle |u_q|^2 \rangle \simeq h^2\frac{\tilde{\lambda}_x + \tilde{\lambda}_z}{\tilde{\lambda}_x\tilde{\lambda}_z}\frac{k_BT}{1+q^2\ell^2}. \quad (12)$$

In our case, higher orders in the expansion in qh must be considered before one can reach any conclusions about the existence of an instability when $\ell^2 < 0$. However, these higher order terms (e.g., terms in q^4) are often positive and stabilizing and we do not expect any instabilities to take place in the systems we consider. Equation (12) nonetheless suggests that the system may show an unusually large response to surface perturbations with wavelengths $\sqrt{-\ell^2}$: this wavelength corresponds to a damped resonance if there is no further instability. Isotropic materials exhibit such a regime when $\nu \to 1/2$ (i.e., for rubberlike materials). Anisotropic materials can reach this regime when either the modulus λ_{xxzz} or the shear coefficient λ_{xzxz} are large. This resonance and the associated large response is probably not relevant for biological systems: the resonant wavelength is of order of the thickness of the material, that is, of the order of a few nanometers in the case of grafted molecules, whereas the applied stresses are usually in the micrometer range.

The previous analysis relies on the assumption that the film is grafted to a rigid substrate, where no displacement takes place on the bottom surface of the film. However, cells develop focal adhesion when the substrate is functionalized with various molecules that can result in either strong or weak grafting condition. It is therefore important to relate the elastic properties of the substrate to the stress-induced deformations. Obviously, if the substrate consists of a three-dimensional elastomer, the finite thickness effects previously discussed are no longer consistent since the surface stress now applies to an effective semi-infinite elastic medium. However, if the surface treatment consists of a coating of molecular thickness that, instead of grafting the film to the surface, causes adhesion via a finite, harmonic adhesive potential, all the former results still hold, but with some modifications [11].

(i) Both the amplitude and the range of force-induced displacements become larger as the strength of the adhesive potential decreases: the effective screening length ℓ, Eq. (11), increases with softer boundary condition on the bottom surface, leading to a larger response.

(ii) However, the amplitude of the variations of surface density can be shown to decrease with the strength of adhesion. In the limit of very low adhesion strength, surface stresses indeed translate the elastic film but do not deform it; the density does not vary.

In conclusion, although semi-infinite, elastic media transmit long-range stresses, the effects of the finite thickness of the layer dramatically reduces this range, transforming the usual power law to an exponential decay whose length scale is given roughly by the balance of the compression and the shear moduli. Releasing the constraint of strong grafting condition and considering instead a finite adhesion energy modifies the range of the exponential decay but does not change the qualitative behavior of the stressed elastic film. Finite thickness also gives rise to the possibility of a regime where the system shows an unusually large response to surface forces (i.e., an elasticity-induced "resonance"); however the relevant wavelength at which this response is large is of order of the thickness of the elastic layer. These predictions could be tested experimentally on polyelectrolyte multilayers, whose elastic moduli can be varied by tuning the ionic strength [19]. The predicted large amplitude deformation regime for Poisson ratio $\nu \lesssim 1/2$ [see Eqs. (16)–(18) for the isotropic case] may then be seen with such materials.

IV. SURFACE ELASTIC ANISOTROPY EFFECTS

Taking into account two-dimensional (x and y) variations of the deformations and the surface stresses adds significant technical complexity to the problem but does not change the qualitative effect of finite thickness-induced short-range elas-

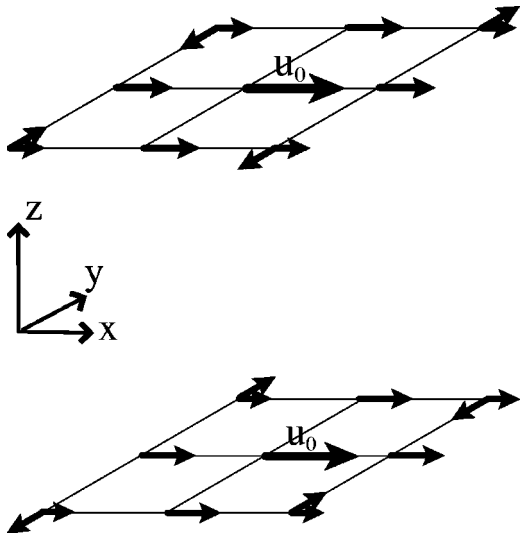

FIG. 2. Response due to the direct (a) and indirect (b) coupling between x and y. The z component of the deformation is not represented.

tic interactions. However, several novel aspects appear such as an effective, in-plane shear modulus that arises from the boundary conditions. We first describe this boundary-induced coupling effect and evaluate its consequences for the surface deformations. In Sec. IV B, we focus on anisotropic elastic media and predict the influence of elastic anisotropy on the symmetry of the response. When considered in the context of cell adhesion, these results suggest that the observed anisotropic growth of sheared adhesive junctions [5] may simply originate from the force-induced, anisotropic deformations of the junctions.

A. Boundary-induced strain coupling

As mentioned before, a fluid monolayer grafted to a surface has no intrinsic, direct coupling between the two planar directions x and y; the elastic energy corresponds to Eq. (1), where $\lambda_{xxyy}=\lambda_{xyxy}=0$. But even without any direct elastic coupling of x and y, a force in the x direction can induce a deformation in the y direction because of the grafting surface boundary condition of zero displacement. Indeed, the x and y direction strains are indirectly coupled through the boundary condition at $z=0$ and via the shear moduli λ_{xzxz} and λ_{xxzz}. A variation of u_x generates a response u_{zz}, but u_{zz} is also coupled to u_{yy} due to the general shear modulus y-z shear modulus (the same argument holds for u_{xz} and u_{yz}). This indirect coupling is responsible for an atypical response of the material: a surface shear stress induces an in-plane compression at the front edge of the stressed region as presented in Fig. 2. However this effect is negligible when the stiffness of the molecules is large (λ_{zzzz} larger than the other elastic coefficients), a situation that can occur in a layer of short molecules grafted to a surface, such as proteins involved in cell-matrix junctions. In such cases, surface forces do not stretch the molecules, which instead respond as solid blocks: $u_{zz}\simeq 0$. No indirect coupling takes place and a surface shear stress only induces a polarized displacement in the direction of the force. For symmetry reason, the displacement u_x in the direction of the force is the same on both sides of the stressed region. But we expect the variations of the surface density of the material to be antisymmetric as it is related to the gradient of the displacement u_x. The relevant parameter that describes the polarization of the response of a layer of proteins to surface shear forces is therefore not the displacement but the variation of surface density:

$$\frac{\delta\Phi}{\Phi} = -(u_{xx}+u_{yy}).$$

Before focusing on anisotropic elastic media that are relevant to the description of adhesive junctions involved in cell adhesion, we first illustrate the indirect coupling effects by looking at the spatial deformation induced by a tangential force $\vec{f}(x,y)=f(x,y)\vec{e}_x$ that stresses the surface of an *isotropic* elastic, thin film. We consider this particular case (as opposed to the anisotropic thin film) in order to simplify the presentation. For the isotropic case, the calculation can be performed in a simple and instructive manner. The situation of isotropic media is however slightly different from an anisotropic thin film or fluid monolayer: in the isotropic case, a direct coupling exists between the planar directions x and y even in the bulk material; that is, the shear moduli λ_{xyxy} and λ_{xxyy} are nonzero even in the bulk. This adds to the indirect coupling between the x and y directions induced by the finite thickness effects as described above. We nonetheless show that both contributions (the direct and the indirect ones) compete; based on this, we can deduce the response of an elastically anisotropic, grafted layer with no direct coupling between x and y, without performing this technically more complex calculation.

Using the same procedure as in the preceding section, we consider the energy of an isotropic film subject to a fixed surface *strain* $\vec{u}(x,y,h)$; later on, we relate this strain to the surface force that induces the surface strain. The energy is then written as

$$\begin{aligned}\mathcal{E} = \frac{E}{2(1+\nu)h}\int\frac{d^2q}{2\pi}\Bigg[&\frac{|u^h_{qx}|^2}{2}[1+q^2h^2(\tilde{\lambda}_1+\tilde{\lambda}_2\cos 2\theta)]\\ &+\frac{|u^h_{qy}|^2}{2}[1+q^2h^2(\tilde{\lambda}_1-\tilde{\lambda}_2\cos 2\theta)]+\frac{|u^h_{qz}|^2}{2}(\tilde{\lambda}_z+q^2h^2\tilde{\lambda}'_z)\\ &+\frac{\tilde{\lambda}_{xy}}{2}q^2h^2\sin\theta\cos\theta(u^h_{qx}\bar{u}^h_{qy}+\bar{u}^h_{qx}u^h_{qy})\\ &+\frac{iqh}{2}\tilde{\lambda}_{xz}[\cos\theta(u^h_{qx}\bar{u}^h_{qz}-\bar{u}^h_{qx}u^h_{qz})+\sin\theta(u^h_{qy}\bar{u}^h_{qz}\\ &-\bar{u}^h_{qy}u^h_{qz})]\Bigg],\end{aligned} \tag{13}$$

with the renormalized elastic coefficients:

$$\tilde{\lambda}_1=\frac{23-56\nu+32\nu^2}{48(1-\nu)(1-2\nu)},\quad \tilde{\lambda}_2\frac{7-8\nu}{48(1-\nu)(1-2\nu)},\quad \tilde{\lambda}_{xy}=2\tilde{\lambda}_2, \tag{14}$$

$$\tilde{\lambda}_z = \frac{2(1-\nu)}{1-2\nu}, \quad \tilde{\lambda}'_z = \frac{(3-4\nu)(1-4\nu)}{12(1-2\nu)^2}, \quad \tilde{\lambda}_{xz} = \frac{4\upsilon - 1}{2(1-2\nu)}, \tag{15}$$

where $\tilde{\lambda}_{xy}$ is the combination of both sources of direct coupling between x and y, λ_{xyxy} and λ_{xxyy}. Contrary to $\tilde{\lambda}_{xz}$ which can change sign because of the opposite action of the compression-induced shear λ_{xxzz} and the shear modulus λ_{xzxz}, $\tilde{\lambda}_{xy}$ is always positive. Indeed, both contributions to the shear λ_{xxyy} and λ_{xyxy} favor the same final state where the material is expanded in the x-y plane at the front of the perturbation and compressed at the rear (see Fig. 2). The minimization of Eq. (13) when a tangential force $\vec{f}=f(x,y)\vec{e}_x$ is applied to the surface leads to the following deformation after Fourier inversion (in the limit $r \gg \ell$):

$$u_x(r,h) \simeq \frac{2(1+\nu)f}{E} * \frac{h^3}{3\ell^4}\sqrt{\frac{\pi}{2}}\frac{e^{-r/\ell}}{\sqrt{r/\ell}}\left(1 + \frac{1+6\nu}{2(1-\nu)}\cos^2\phi\right), \tag{16}$$

$$u_y(r,h) \simeq \frac{2(1+\nu)f}{E} * \frac{h^3}{\ell^4}\sqrt{\frac{\pi}{2}}\frac{e^{-r/\ell}}{\sqrt{r/\ell}}\cos\phi \sin\phi \frac{1+6\nu}{6(1-\nu)}, \tag{17}$$

$$u_z(r,h) \simeq \frac{2(1+\nu)f}{E} * \frac{h^2}{\ell^3}\sqrt{\frac{\pi}{2}}\frac{e^{-r/\ell}}{\sqrt{r/\ell}}\cos\phi \frac{4\nu-1}{4(1-\nu)}. \tag{18}$$

In this expression, (r,ϕ) are the polar coordinates on the surface of the medium while * indicates a convolution as defined by Eq. (9) but extended to two dimensions. These formulas show the same trend as we found in the preceding section where only one surface dimension was considered: the deformation decays exponentially on a length scale ℓ, defined here as $\ell = h\sqrt{(23-48\nu)/[24(1-\nu)(1-2\nu)]}$. Note that ℓ is still not well defined close to $\nu=0.5$ where one must include terms higher order in the wave vector. Our expansion is indeed not precise enough to explore this region, but the previous stability analysis still holds and predicts an increased sensitivity of the film to perturbations with wavelengths close to $\sqrt{-\ell^2}$ when the elastic parameters are such that $\ell^2<0$. The deformations for this two-dimensional case are not isotropic in the x-y plane, but the anisotropy of the deformation is insensitive to the film thickness. The deformation described by Eqs. (16)–(18) shows the same angular dependance as one finds for surface stresses on a semi-infinite elastic medium [12]. The in-plane displacement takes place mainly in the direction of the force ($\phi=0$), similar to the behavior in a semi-infinite medium. As a consequence, the variations of the density $\delta\Phi/\Phi = -u_{xx}$ are also highly anisotropic. A localized force, mathematically represented by a Dirac δ function, leads thus to

$$\frac{\delta\Phi}{\Phi} \simeq \frac{F}{E}\left(\frac{h}{\ell}\right)^3 \frac{(1+\nu)(3+4\nu)}{6(1-\nu)}\frac{e^{-r/\ell}}{\sqrt{r/\ell}}\cos\phi \tag{19}$$

to first order in ℓ/r. The dependence on $\cos\phi$ in Eq. (19) predicts a highly anisotropic response to force: the density mainly varies in the direction of the force and not perpendicular to it. As emphasized in Sec. IV B, specific anisotropic elastic properties of materials can enhance this feature and lead to an even more directional response, where u_y is completely negligible. This anisotropic deformation is the effect we suggest as the origin of the polarized biochemical response of cell adhesion under stress, where new proteins aggregate to the adhesive junction specifically at the front edge.

Although it is not apparent in Eq. (17), the sign of the prefactor of u_y comes from the competition between the direct and the indirect coupling between x and y: $u_y \propto (\tilde{\lambda}_{xy}\tilde{\lambda}_z - \tilde{\lambda}_{xz}^2)/\tilde{\lambda}_z$. The direct coupling $\tilde{\lambda}_{xy}$ is responsible for the intuitive response: a displacement of a spot in the positive x direction expands the elastic medium in the y direction in front of the spot ($x>0$) and a compression in the negative x direction. The effect of the indirect coupling causes a nonintuitive deformation due to the ability of the material to use the z direction to move material toward the stressed region at the front edge and away from it at the rear (Fig. 2); a local force induces a compression in the x-y plane at the front edge of the stressed region and expansion behind it. Finally, the direct and indirect couplings between x and y compete so that a deformation along the x direction is expected to induce a smaller response in the y direction for an isotropic material compared with an anisotropic, thin fluid layer, where no direct coupling balances the finite thickness-induced shear deformation.

B. Elastic anisotropy effects on deformations

The situation for anisotropic, fluid grafted layers can be deduced from the isotropic case. Since $\tilde{\lambda}_{xy}=0$, we expect the material to be compressed in the x-y plane at the front edge of the perturbation, contrary to the intuitive expectation [Fig. 2, case (b)]. The sign of the displacement in z is as before dependent on the relative contribution of the shear coefficients λ_{xxzz} and λ_{xzxz} and will lead either to an expansion in the z direction when $\lambda_{xxzz} > \lambda_{xzxz}$ or to a compression in the opposite case. A situation of interest that can be easily predicted is the very anisotropic case where stretching the grafted molecules is very costly energetically: λ_{zzzz} is larger than any other elastic coefficient. As mentioned before, this assumption is relevant to describe layers of proteins bounded to a surface such as the ones involved in cell-matrix junctions. Because λ_{zzzz} is large, a surface force $\vec{f}(x,y) = f(x,y)\vec{e}_x$ results in negligible stretching of the molecules in the z direction, and the indirect coupling between the in-plane directions that arises from finite thickness effects becomes negligible. Due to this anisotropy, the force-induced displacement is, to a good approximation, in the direction of the force (u_y and u_z scale like $1/\lambda_{zzzz}$):

$$u_x(x,y,h) \simeq \frac{f(x,y)h}{\lambda_{xzxz}} * \pi \frac{e^{-|x|/\ell}}{\ell} \delta(y), \tag{20}$$

where $\ell = \sqrt{\lambda_{xxxx}/3\lambda_{xzxz}}$ is the typical range of deformation and $\delta(y)$ is the one dimensional Dirac function. Equation (20) shows that for a constant force $\vec{f} = f\vec{e}_x$ applied on a rectangle of size $2L_x \times 2L_y$, the deformation is only significant at the edges normal to the force whereas the lateral sides are perturbed in a negligible way. This anisotropic variation of the surface density shows how the boundary conditions of surface attachment result in a shearlike response of an initially fluid layer to a directional surface stress. Outside of, but close to the stressed rectangle,

$$\frac{\delta\Phi}{\Phi} = -(u_{xx} + u_{yy}) \simeq \frac{f\,h}{\lambda_{xzxz}\,\ell}[H(L_y - y) - H(-L_y - y)]\sinh\frac{L_y}{\ell}\, e^{-|x|/\ell}\mathrm{sgn}(x), \tag{21}$$

where H is the step function (also called Heaviside function). When considered in the context of biological cell-matrix junctions, Eq. (21) shows that a constant surface force applied onto a layer of stiff, grafted molecules induces an in-plane compression of range ℓ at the front of the layer as well as an in-plane expansion of range ℓ at the back edge of the stressed zone; negligible deformations are expected on the sides. Adhesive junctions are indeed observed to respond to forces with an increase of their size in a highly anisotropic manner; new proteins aggregate at the front edge [5] and not at the back nor the sides. This behavior is consistent with our suggestion that the anisotropic elastic response of the thin layer of proteins to the surface stresses originating from cytoskeleton-induced cell contractility triggers spatially localized biochemical reactions; the anisotropic change in the density of the protein layer due to the surface stress may make it more favorable for additional proteins to aggregate at the front of the layer but not at the sides or back. This provides a link between the elasticity-induced in-plane compression to the biochemical response.

In conclusion, surface stresses applied to grafted layers of molecules create short-range perturbations whose range is limited to the film thickness. Finite thickness and the grafting boundary condition induce an effective shear response to surface stresses, so that even fluidlike layers become sensitive to shear. A localized surface stress also induces perturbations in directions perpendicular to the stress even for cases where there are no direct elastic coupling between the x and y directions inthe bulk system. On the contrary, for cases where the system possesses an intrinsic x-y shear modulus, the surface grafting boundary condition *decreases* the effect of the direct elastic coupling that exists for isotropic elastic media, leading to a more directional perturbation. Both the short-range effect of stress forces and the boundary-induced directionality may explain the mechanosensing observed in biological cell adhesion as a local, anisotropic elastic process that generates a highly directional, biochemical response.

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