Deflection of a cell membrane under application of a local force

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If a localized force or torque (caused by an integral protein, a receptor, a cantilever of the atomic force microscope, a cell-kicking instrument, and so on) is applied to the surface of a cell membrane it is deflected in a small region. Equations describing the statics and dynamics of small local deflections of the cell membrane are deduced and the Green function of the state equation is calculated. The force-displacement dependence for an atomic force microscope in the regime of small indentation is discussed. [S1063-651X(98)07702-2]

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The mechanical behavior of cell membranes attracts a strong interest. We consider here such kinds of cells as animal cells and *Dictyostelium discoideums*. These cells exhibit a composite membrane consisting of a lipid bilayer and associated integral proteins. The bilayer is attached to a cellular cytoskeleton. The latter may consist of a membrane coupled actin-spectrin network, which is connected with the bulk cellular cytoskeleton (Fig. 1).

Membranes of animal cells can be considered as shells. It is common knowledge that in some cases there can exist special types of bending that are not followed by stretching of a shell. Since the membrane bending energy is small with respect to that of stretching, if the shell admits such kind of deformation it actually takes place [1]. Therefore in the case of a biological membrane, its deformation is believed to take place by way of either pure bending or in-surface shear deformation due to small values of the bending rigidity and the shear modulus [2–4]. In the case of vesicles their bending is successfully described by the Helfrich curvature elasticity model [2] or its modifications [3]. If a shell is subjected to deformation with finite stretching, the so-called ''membrane shell theory'' can be applied in which bending moments are neglected [1]. This approach was applied by Evans and Skalak to the case of red blood cells [4].

The opposite situation takes place when local membrane inhomogeneities, normal local forces or torques applied to a cell, are studied, since in this case local bending cannot take place without local stretching, the contributions of bending and stretching energies having the same order of magnitude. (See Ref. [1]. See also the discussion in this paper later on.) If application of a local force causes a finite membrane deformation its state can be described by the ''membrane shell theory'' taking into account moment resultants [4]. The latter is, however, rather complicated, especially if one is interested in distribution of both force and membrane deflection.

For several reasons a description of local bending of cell membranes is of considerable interest. First of all, new experimental (micromechanical) techniques for local deformation studies of cells are available now, while studies of global deformations are hardly possible yet. The latter are very sensitive to details of loading geometry and boundary conditions since their contributions vanish only slowly with distance [1]. In contrast, more simple local measurements in which deflections vanish on distances small with respect to the shell size are not too sensitive to global details of experimental geometry.

Some local micromechanical experimental methods, such as the cell-kicking method [5], magnetic tweezers [6], cell poking [7], and atomic force microscopy [8,9] are successfully applied to study cells. Interpretation of these experiments requires a theoretical description of local membrane deformation.

In addition, there have been many experimental observations of local phenomena in cell membranes: budding, blebbing, arising of invaginations, and caveolae [10]. Finally, cell membranes experience local bends on a mesoscopic scale in processes with the participation of integral proteins, membrane receptors, enzymes, and so on. Understanding these phenomena requires equations describing small deflections of cell membranes under applications of local forces and/or torques.

The aim of the present communication is to deduce the free energy, and the state and dynamic equations of a cell membrane suitable to describe its small local deflections. Cell membranes are usually considered as thin shells.

It is generally accepted that for cell membranes $k \sim \lambda h^2$ [11], where k is the membrane bending modulus, λ is its

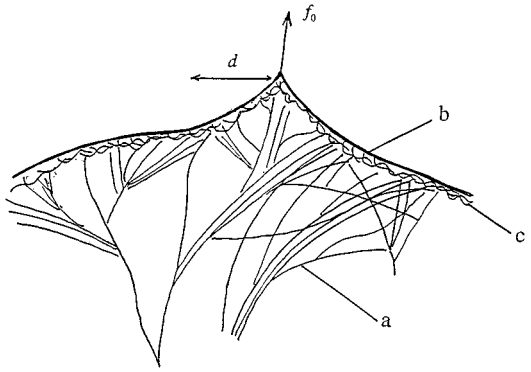

FIG. 1. Schematic representation of a deflection of a cell membrane under application of a localized force $f_0 \cdot d$ is the dimension of the deflection region. (a) The bulk cytoskeleton, (b) the lipid membrane, (c) the submembranous actin network.

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second Lame coefficient describing the lateral stretching elasticity [12], and h is the membrane thickness. Let d be the lateral dimension of the bending region. The bending and stretching energies F_b and F_{st} can be estimated as $F_b \sim k\psi^2 d^{-2}$ and $F_{st} \sim \lambda \psi^2 d^2 R^{-2}$, where ψ is the membrane deflection. The order of magnitude of d is given by the condition where the sum of these energies is a minimum, whence $d \sim (hR)^{1/2}$. Taking $h \sim 10^{-9}$ m, $R \sim 10^{-5}$ m one gets $d \sim 10^{-7}$ m and $d/R \sim 10^{-2} \ll 1$. One finds the energies of bending and stretching to be of the same order of magnitude $F_b \sim F_{st} \sim \lambda \psi^2 h R^{-1}$. This means that under application of a localized force membrane local bending is always accompanied by its stretching and in order to describe the phenomenon one should take into account both contributions.

Several models are used to describe the bending energy of lipid bilayers (Refs. [2,3]). It is believed that it is well described by the Helfrich bending energy:

$$F_b = \int \left[\frac{k}{2} (c_1 + c_2 - c)^2 + \sigma \right] dA + p_0 \int dV \qquad (1)$$

with the spontaneous curvature c and the main curvatures c_1 and c_2. p_0 and σ are the difference between the outer and the inner pressure $p_0 = p_{out} - p_{in}$ and the tensile stress, A is the surface area. In the case of vesicles k, c, p_0 and σ characterize the properties of the lipid bilayer and its environment. They are considered to be independent of surface coordinates and time.

In the case of a cell membrane the bending modulus, spontaneous curvature, and surface tension can vary along the surface. In general they depend on time. In this case they describe the properties of the whole cell membrane with its complex structure in a phenomenological way rather than only of the lipid bilayer. Whereas erythrocyte has a smooth surface [4,11], another kind of eukariotic cell (in particular leukocytes and endothelial cells) possess a store of membrane surface in folds, buds, blebs, and ruffles [13]. Most cells have internal membranes and vesicles. The latter can join to the cell membrane and fuse when it needs the material (or break away from it in the opposite case). In the case of erythrocytes the characteristic time of this process is about a few hours [4]. However, for the other kind of cells it can be much smaller. Recent experiments with *Dictyostelium discoideums* showed that numerous internal vesicles fused to the cell membrane under aspiration of a part of its surface into the micropipet, which was followed by jumpwise increases of the surface of the aspirated cell part. The characteristic time necessary for the individual vesicle to join the membrane and fuse was observed to be of the order of 0.1–1 s [14]. In the case of this kind of cell in experiments lasting from several minutes to hours one should take into account the existence of internal reservoirs of the membrane surface. Besides, lipids and other membrane molecules can be synthesized or metabolized by an active cell. Thus the usual constraints for vesicles of a constant surface area and volume cannot be applied here and in the case of a cell σ plays the role of a ''chemical potential of the membrane area'' describing the property of the area reservoir and p_0—the pressure difference rather than the Lagrange multipliers.

The cell membrane possesses a lateral elasticity with lateral elastic moduli λ and μ (which in general are also coordinated and time dependent). Consider a locally isotropic membrane. The contribution of the stretching elasticity to the cell free energy F_{st} takes the form [15]

$$F_{st} = \int \frac{\lambda + \mu}{2} (\delta A/A)^2 dA. \qquad (2)$$

Here δA is the variation of the surface area under stretching [16].

Consider a membrane that is described by the radius vector $\mathbf{R}$ of the points on its surface. Under application of a localized force that is normal to the membrane surface the main contribution to the small membrane displacement is made by its normal component $\Psi = \Psi(\mathbf{R})$. Under a deflection the new radius vector of the surface $\mathbf{R}'$ can be thus defined as $\mathbf{R}' = \mathbf{R} + \mathbf{n}\Psi$, where $\mathbf{n}$ is the surface outer normal [17]. Though all results can be obtained in a general case (not fixing the surface shape), we consider here the case of a cell, which is initially spherical (with the radius $|\mathbf{R}| = R$) for which all the expressions take the simplest form.

The inner part of most of animal cells contains a bulk cytoskeleton composed of filaments—actin fibers, intermediary filaments, and microtubuls. The filaments form a branching and interlacing meshwork that connects with microtubuls, nuclei, organelles, and the network near the cell borders [18]. We take into account two contributions of the bulk cytoskeleton to the membrane energy. First, the cytoskeleton can produce a pressure $p_{cyt} = p_{cyt}(\mathbf{R})$ onto the membrane inner surface. Second, the cytoskeleton has its own rigidity, which can be roughly characterized by a Young's modulus E_{cyt} and a Poisson's ratio v_{cyt}. Deflection of the cell membrane is followed by deformation of the bulk cytoskeleton (Fig. 1). The energy of its deformation must be also included in the membrane energy. The contribution of the cytoskeleton to the membrane energy can be roughly taken in the form

$$F_{cyt} = \int \left(-p_{cyt}\Psi + \frac{E_{cyt}}{2(1-2v_{cyt})R} \Psi^2 \right) dA. \qquad (3)$$

Cell membranes contain different impurities dissolved in the bilayer such as integral proteins. Integral proteins can give rise to torques bending the membrane. In the case of a flat symmetric lipid bilayer inclusion can cause its local bending only if the inclusion is asymmetric with respect to the bilayer, while symmetric proteins have no effect on deflection of the flat symmetric membrane [19]. In contrast, in the curved and structurally asymmetric cell membrane, each sort of integral protein gives rise to a local torque. The latter can be described by the dependence of the spontaneous curvature c on the surface coordinates $\mathbf{R}$: $c(\mathbf{R}) = c_0 + \delta c(\mathbf{R})$, where c_0 is a constant. It plays the role of the spontaneous curvature of the cell membrane far from integral proteins. The lateral size of integral proteins is typically $L \sim 10^{-8}$ to 10^{-9} m. Since $L \ll d$ one can represent $\delta c(\mathbf{R})$ as $\delta c(\mathbf{R}) = a\,\delta(\mathbf{R})$, where a is a constant describing the power of the internal torque induced by the individual integral protein and $\delta(\mathbf{R})$ is the δ function on the surface. The bending rigidity of integral protein is different with respect to that of the membrane, hence it changes locally the membrane bending modulus [20]: $k = k_c + b\,\delta(\mathbf{R})$, where k_c is the bending modulus of

the membrane far from impurities and b is a constant. Insertion of a new protein into the cell membrane results in a local membrane dilatation $s\delta(\mathbf{R})$ (where s is a protein lateral area) in addition to the dilatation that is caused by the membrane bending. The latter is obtained in Ref. [17]. The effective dilatation $\delta A/A$ takes the form

$$\frac{\delta A}{A}=s\delta(\mathbf{R})+(c_1+c_2)\Psi+c_1c_2\Psi^2+g^{ij}\nabla_i\Psi\nabla_j\Psi/2 -\{(c_1+c_2)g^{ij}+c_1c_2L^{ij}\}\Psi\nabla_i\Psi\nabla_j\Psi, \quad (4)$$

where ∇_i is the covariant derivative along the surface, g^{ij} is the surface metric tensor, and L^{ij} is the surface second fundamental form tensor (the definitions of g^{ij} and L^{ij} and some details one can find in Ref. [17]). In the case of a spherical surface they have the form $g^{11}=R^{-2}$; $g^{22}=(R\sin\theta)^{-2}$; $g^{12}=g^{21}=0$; $L^{11}=-R^{-3}$; $L^{22}=-R^{-3}\sin^{-2}\theta$; and $L^{12}=L^{21}=0$, where θ is the spherical polar angle. Finally, if a local force $\mathbf{f}=\mathbf{f}_0\delta(\mathbf{R})$ is applied to an integral protein, to a receptor or directly to the membrane one has to take into account its work, which takes the form $W=\int(\mathbf{fn})\Psi\ dA$.

Now let us consider nonlinear contributions (proportional to Ψ^3 and Ψ^4) to the free energy. The latter must be taken into account when local shape bifurcations are studied or in the case of nonharmonic deformation. The contribution $\sim\Psi^3$ originating from F_b was obtained in Ref. [17]. The free energy must be positively defined (Ref. [25]) and thus one should extend the expansion at least up to the fourth degree in Ψ. The latter term was not obtained yet for a membrane of a general shape. Assume that it is the geometrical nonlinearity that makes the main contribution to the free energy. In this case it is possible to find the main terms of the third and fourth orders in Ψ. One has two contributions to the nonlinear terms. The first of them arises due to the bending energy F_b Eq. (1). The dimensional considerations show that the main terms of the third and fourth order that appear in the expansion of the energy F_b (1) can be estimated as $k_c\Psi^3R^{-1}d^{-4}$ and $k_c\Psi^4R^{-2}d^{-4}$. The main terms of the contribution of the stretching energy $F_{\rm st}$ [Eq. (2)] with $\delta A/A$ given by Eq. (4) are the order of $(\lambda+\mu)\Psi^3/Rd^2$ and $(\lambda+\mu)\Psi^4/d^4$. It is easy to verify that the two latter terms are much larger than the two former ones.

The free energy has the form $F=F_b+F_{\rm st}+F_{\rm cyt}-W$. Making use of the above considerations one gets the expression of the free energy describing small local deflections of a cell membrane:

$$F=\int\left\{\frac{1}{2}\Psi(k_c\Delta^2\Psi+B\Delta\Psi+D\Psi)-q(\mathbf{R})\Psi +(\lambda+\mu)\left[\frac{\Psi g^{ij}\nabla_i\Psi\nabla_j\Psi}{R}+\frac{(g^{ij}\nabla_i\Psi\nabla_j\Psi)^2}{8}\right]\right\}dA, \quad (5)$$

where Δ is the Laplace-Beltrami operator on the sphere, $B=pR/2+k_c(2+c_0R)R^{-2}$; $D=pR^{-1}+2k_cc_0R^{-3}+4(\lambda+\mu)R^{-2}+E_{\rm cyt}(1-2y_{\rm cyt})^{-1}R^{-1}$; $p=p_{\rm cyt}+p_0=p_{\rm cyt}+p_{\rm in}-p_{\rm out}$. The function $q(\mathbf{R})=q\delta(\mathbf{R})$ with $q=2k_c(1-c_0R)R^{-2}a-2(\lambda+\mu)R^{-1}s-(2-c_0R)R^{-2}b+(\mathbf{f}_0\cdot\mathbf{n})$ is determined by the properties of the impurities. We assume a, b, s, and the force $\mathbf{f}_0$ to be small and to give rise to a small deflection ψ of the membrane. Hence the product $q\psi$ is of the second order of magnitude $q\psi\sim\psi^2$. q plays the role analogous to that of a charge in electrostatics, therefore in what follows it is referred to as ''elastic charge'' [24].

In the case of a local displacement caused by the localized force in order to describe the membrane stretching it is sufficient to consider the linear part of Eq. (4) (with $s=0$), which has the form $\delta A/A=(c_1+c_2)\psi$ since the tangential surface displacement is small. It shows that under the applied localized force the local bending of a curved membrane is always followed by its local stretching (if $c_1+c_2\neq0$). This phenomenon manifests itself only due to the surface curvature and in the flat case $c_1\to c_2\to0$ ($R\to\infty$) it disappears. At first glance it seems to contradict the condition of a constant total area usually applied in the theory of vesicles [3,17]. In principle Eq. (4) is consistent with the constraint $\oint dA=$const. The latter condition, being applied to the membrane together with Eq. (4), demands the membrane deformation be nonlocal. However, the condition $\oint dA=$const is an approximation resulting from the *a priori* assumption that this constraint gives a minimum to the total energy. As we have discussed above, in the case of the local deflection caused by the localized force the correct approach is to take into account both the stretching and the bending energies and to demand that the total free energy Eq. (5) is a minimum, rather than to use the approximation $\oint dA=$const.

Note that the structure of the square part of the free energy Eq. (5) is completely prescribed by the membrane symmetry. Namely, for the spherical membrane it always has the form $\oint\frac{1}{2}\psi(k_c\Delta^2\psi+B\Delta\psi+D\psi)dA$ with k_c, B, and D unequal to zero. This form of the free energy takes place already in the case of a spherical vesicle (which has neither cortex nor cytoskeleton) (Ref. [17]). Therefore it is of interest to understand what mechanisms make contributions to these constants in the case of an animal cell. The solution is given by Eq. (5). It is also important to estimate relative values of these constants.

Relations between the values of the parameters usually met in experiments make it possible to simplify the expression for the free energy. For cell membranes $\lambda\gg\mu$ [4,11]. The order of magnitude of the bending modulus is $k_c\sim10^{-19}$–10^{-20} J [4]; the lateral elastic moduli $\lambda\sim10^{-5}$ J/m^2 for flaccid erythrocytes [4], $\lambda\sim0.3$ J/m^2 for swollen erythrocytes [21] and $\lambda\sim10^{-4}$ J/m^2 for unfertilized sea urchin egg. $c_0\sim R^{-1}$; $R\sim10^{-5}$ m. The membrane surface tension can take values between zero and $\sigma\sim10^{-5}$ J/m^2 [21,22] and the corresponding pressure difference—between zero and $p\sim10$ Pa. $E_{\rm cyt}\sim10^3$–10^5 Pa [8]. Consider the regime of a small value of the pressure difference $p\approx0$. In this case using the above estimations one gets $D\sim10^9$ to 10^{10} J/m^4; $B\sim10^{-10}$ J/m^2. Estimating $\Delta\psi\sim\psi d^{-2}$ one gets $k_c\Delta^2\psi\sim D\psi\gg B\Delta\psi$ and $d\sim\{k_c/D\}^{1/4}\sim10^{-7}$ m. Thus the term $B\psi\Delta\psi$ of the free energy Eq. (5) can be omitted [23]. The quadratic part of the free energy takes the form

$$F=\int\{\tfrac{1}{2}k_c\psi\Delta^2\psi+\tfrac{1}{2}D\psi^2-q(\mathbf{R})\psi\}dA. \quad (6)$$

Note that the elastic charge $q\delta(\mathbf{R})$ describes one isolated

protein or a local force. One can consider also a general case with distributed proteins or a distributed force $q=q(\mathbf{R})$.

The inequality $d \ll R$ enables us to make a further simplification in the expression for the membrane energy, which we refer to as the quasiflat approximation. It is easy to prove that under the condition of local bending $d \ll R$ one can use the free energy Eq. (6) as if it were defined on a plane with the Laplace operator $\Delta\psi \approx \partial^2\psi/\partial x^2 + \partial^2\psi/\partial y^2$ and the area element $dA \approx dx\, dy$, where x and y are the in-plane Cartesian coordinates. Since the integral converges one can extend the integration in Eq. (6) up to infinity.

The motion of the membrane is mainly controlled by the energy dissipation by the surrounding water [26]. Besides, the membrane is connected with the internal cell organelles and one should expect that this also makes its contribution to dissipation. The whole phenomenon therefore can be taken into account in a phenomenological way by introduction of the dissipative function Q of the cell membrane: $Q = \frac{1}{2}\int \gamma(\partial\psi/\partial t)^2\, dA$, where γ is the kinetic factor and t is the time. The value of the dissipative factor γ can be estimated within the assumption that energy dissipation by water makes the main contribution to the dissipative function. In the flat geometry $\gamma = \eta q$ where η is the viscosity of water ($\eta \sim 10^{-3}$ J s/m^3) and q is the wave vector [26]. As accurate as it can be obtained within the quasiflat approximation one can take $q \sim d^{-1}$ and get $\gamma \sim \eta/d \sim 10^4$ J s/m^4. This estimate gives a lower limit of the value of γ since it does not take into account dissipation by cytoskeleton. In fact, one should probably expect that it is just the cytoskeleton that makes the main contribution to dissipation of the membrane energy in animal cells and that its contribution can be several orders of magnitude larger than that of water. However, at the moment it is not enough information to estimate it.

The equation of motion can be obtained by making use of the variation principle for dissipative systems $\delta Q/\delta(\partial\psi/\partial t) = -\delta F/\delta\psi$ [25]. In the linear approximation it takes the following form:

$$\gamma \frac{\partial\psi}{\partial t} = -k_c\Delta^2\psi - D\psi + q(r). \tag{7}$$

Within the quasiflat approximation Eq. (7) is considered on the infinite plane: $\mathbf{r}=(x,y)$ is the in-plane radius vector. In the steady state the membrane displacement is subjected to a simple equation of equilibrium:

$$k_c\Delta^2\psi + D\psi = q(\mathbf{r}). \tag{8}$$

One can try its solution in a form of the Fourier integral $\psi(r) = \int \psi_q \exp(i\mathbf{q}\cdot\mathbf{r}) d^2q/(2\pi)^2$:

$$\psi(\mathbf{r}) = \int \frac{q_q \exp(i\mathbf{q}\cdot\mathbf{r})}{k_c q^4 + D} \frac{d^2q}{(2\pi)^2}, \tag{9}$$

where $q_q = \int q(\mathbf{r})\exp(-i\mathbf{q}\cdot\mathbf{r}) d^2r$. The solution (9) is valid in a general case of distributed elastic charge $q(\mathbf{r})$ (distributed integral proteins or of some distributed force). In the case of an isolated protein or of a localized force the elastic charge takes the simple form $q(\mathbf{r}) = q\,\delta(\mathbf{r})$. In this case the deflection is proportional to the Green function $G(r)$ of Eq. (8):

$$\psi(\mathbf{r}) = qG(r), \tag{10}$$

where the Green function is expressed in terms of the Kelvin function $\mathrm{kei}(r/d)$:

$$G(r) = \int \frac{\exp(i\mathbf{q}\cdot\mathbf{r})}{k_c q^4 + D} \frac{d^2q}{(2\pi)^2} = -\frac{d^2}{2\pi k_c}\,\mathrm{kei}(r/d). \tag{11}$$

The dimension d of the bending region is $d = (k_c/D)^{1/4}$. The deflection amplitude $\delta = \Psi(0)$ caused by the local force or by the isolated protein has the form

$$\delta = \frac{q}{8\sqrt{k_c D}}. \tag{12}$$

We estimate the range of the deflection amplitude in which the quadratic free energy Eq. (6) and corresponding

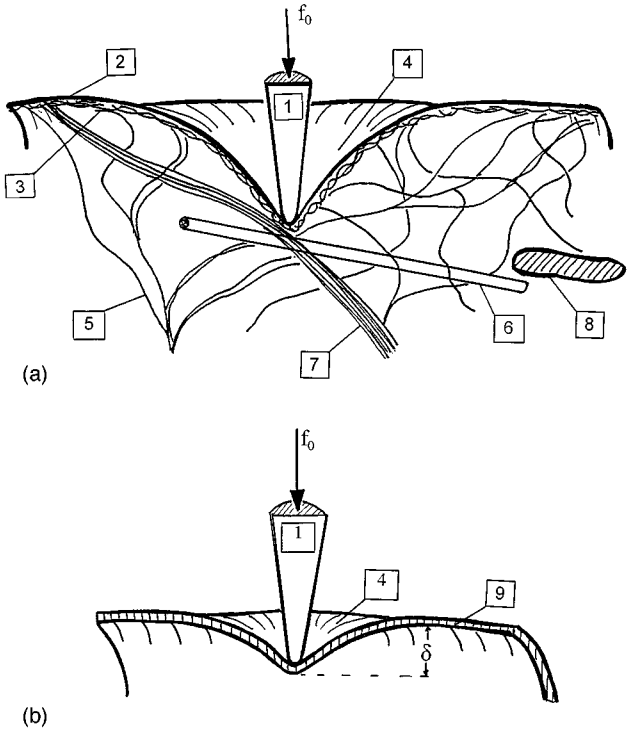

FIG. 2. Schematic view of action of atomic force microscope cantilever on the surface of (a) animal cell and (b) bacterial cell. 1: the cantilever to which the force f_0 is applied; 2: the animal cell membrane with the cortex (3); 4: the deflection region of the membrane; 5: the filamentous part of the cytoskeleton (consisting of actin and intermediate filaments); 6: the microtubule; 7: the actin bundle; 8: the intracellular organelle. Since the effective spring constant of the animal cell membrane is much smaller than that of the cantilever $k_m \ll k_{\mathrm{AFM}}$, in order to balance the force f_0 applied to the cantilever the membrane displacement should be large. The cantilever meets some relatively rigid cell organelle (8), microtubule (6) or actin bundle (7) well before this magnitude of displacement is reached. Therefore presently the atomic force microscope method is unable to characterize the animal cell membrane properties, but it makes it possible to distinguish the rigid part of the cytoskeleton and cell organelles. In contrast, (b) the bacterial wall (9) is much more rigid. It is able to balance the force applied to the cantilever (1) by its own elasticity and bacterial internal pressure. Since $k_w \gg k_{\mathrm{AFM}}$ one can study the bacterial wall elastic properties with the atomic force microscope.

linear equations (7) and (8) are valid. Under the condition $k_c\psi\Delta^2\psi\sim D\psi^2\gg(\lambda+\mu)\psi^3/Rd^2$, $(\lambda+\mu)\psi^4/d^4$ the nonharmonic terms can be neglected. If the cytoskeleton is soft ($E_{\rm cyt}\sim10^3$–10^4 Pa) the limitation for the ratio of the deflection to the cell radius $\psi/R\ll(d/R)^2\sim10^{-4}$ is given. In the case of a rigid cytoskeleton ($E_{\rm cyt}\sim10^5$ Pa) one gets the limitation $\psi/R\ll10^{-1}$–10^{-2}. Note that in the case of a swollen erythrocyte there exists one additional limitation of the application of the above theory since its membrane breaks under dilatation of few percent [4]. This gives the limitation condition $\psi/R<10^{-2}$. For a flaccid erythrocyte and for a cell with a reservoir of surface area this limitation is not valid. Thus though the above approach can be applied for each kind of cell, the range of deflection amplitude is wider in a rigid cell region.

The atomic force microscope data are usually handled using the Hertz approach to the contact problem [1], which considers the cantilever and the cell as homogeneous elastic solids [27,28]. In the case of cells this approach gives a good approximation if the bulk elastic energy of the cell deformation under indentation is much larger than the energy of bending of the cell membrane. The membrane spring constant $k_m=f_0/\delta=8\sqrt{k_cD}$ can be estimated as $k_m\sim10^{-4}$ N/m. This is smaller than the spring constant $k_{\rm AFM}$ of the atomic force microscope cantilever (in modern cantilevers the value $k_{\rm AFM}\sim10^{-3}$ N/m is reached [29]), therefore in the present state of art the contribution of the membrane of animal cells to the cantilever displacement cannot be measured by atomic force microscopes [Fig. 2(a)]. The present-day atomic force microscope is sensitive to the membrane properties in the case of a much more rigid membrane as those of bacteria [Fig. 2(b)]. Making use of the Young's modulus $\sim10^{10}$ Pa and width $\sim10^{-8}$ m of the sheath of the *Methanospirillum hungatei* bacteria [30] one gets the estimate $k_w\sim1$ N/m of the effective spring constant of the bacteria wall. In this case the present approach should be applied.

To summarize, we obtained simple dynamic and static equations describing the small local deflections of the cell membrane under the action of a local force or a local torque and discussed the possibility of application of this approach to atomic force microscope experiments.

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[12] Here the usual notation for the second Lame coefficient λ and the shear modulus μ is kept. λ is related to the compressibility modulus K as $\lambda=K-2\mu/3$. Note that all these values λ, K, and μ are integrated over the membrane width h (Ref. [1]). For membranes λ and K are usually much larger than μ (Refs. [2, 11]).

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[24] Note that the elastic charge q is independent of the angle φ. Dependence of the parameters, a, s, and f_0 on φ should be introduced in order to take into account the possible in-plane asymmetry and the tilt of integral proteins. The tilt takes place in particular under interaction of two proteins (Ref. [20]). For the sake of simplicity this dependence is neglected here. This approach also does not take into account the phenomena arising due to the hydrophobic mismatch (Ref. [19]).

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