Support Materials 1

Definition of the symbols used in paper:

E_m Young's modulus of membrane
E_c Young's modulus of cytoskeleton
F force
R_0 radius of the uncompressed cell

ε relative deformation
ν_m Poisson ratio of membrane
ν_c Poisson ratio of cytoskeleton

Support Materials 2

In our model, prior to compression living cell mechanical structure is approximated as a spherical impermeable elastic balloon (spherical membrane). This balloon is filled with an incompressible fluid and gel-like materials.

Calculation of fluid-filled impermeable spherical membrane deformation between parallel plates assumes that under small deformations the lateral part of membrane extends spherically (except contact regions) [46]. Then, using the volume conservation, the lateral radius of the membrane after deformation, R, can be calculated from the initial membrane radius R_0 and relative deformation ε:

$$R = R_0 + \frac{R_0}{2}\varepsilon^2 \quad \textbf{(A1)}$$

The energy of the stretching of the membrane G with thickness h according to elastic theory is:

$$G = \frac{h}{2}\int u_{\alpha\beta}\sigma_{\alpha\beta}dS \quad \textbf{(A2)}$$

where integration is over membrane surface, $u_{\alpha\beta}$ is two-dimensional deformation and $\sigma_{\alpha\beta}$ is two-dimensional deformation stress tensors:

$$\sigma_{\alpha\beta} = \frac{E_m}{1-\nu_m{}^2}[(1-\nu)u_{\alpha\beta} + \nu\delta_{\alpha\beta}u_{\gamma\gamma}] \quad \textbf{(A3)}$$

where E_m is Young's modulus, ν_m is Poisson ratio of membrane, and summation must be over repeating indices.

Balance of stress defines the pressure inside the balloon:

$$P = \frac{h}{R}(\sigma_{\theta\theta} + \sigma_{\phi\phi}) \quad \textbf{(A4)}$$

Using the relation between stress and deformation tensors,

$$\begin{aligned} Eu_{\theta\theta} &= \sigma_{\theta\theta} - \nu\sigma_{\phi\phi} \\ Eu_{\phi\phi} &= \sigma_{\phi\phi} - \nu\sigma_{\theta\theta} \end{aligned} \quad \textbf{(A5)}$$

and the assumption that the deformed balloon has a spherical shape, yields

$$u_{\phi\phi} = u_{\theta\theta} = \frac{u_r}{r} = \frac{r - r_0}{r_0} \quad \textbf{(A6)}$$

and the stress tensors

$$\sigma_{\phi\phi} = \sigma_{\theta\theta} = \frac{E_m}{1-\nu}\frac{r - r_0}{r_0} \quad \textbf{(A7)}$$

Substituting Eq. A6 and Eq. A7 to Eq. A2, we obtain the elastic energy of the spherical membrane stretching:

$$G_{el} \approx 4\pi \frac{E_m}{1-\nu_m}(r - r_0)^2 \quad \textbf{(A8)}$$

Correspondingly, the reaction force (load)

$$F_{el} = -\frac{\partial G_{el}}{\partial Z} = 2\pi \frac{E_m}{1-\nu_m} h R_0 \varepsilon^3 \quad \textbf{(A9)}$$

has cubic dependence on relative deformation ε.

Note that membrane bending was ignored. For bending of the noncontact area of a spherical membrane, the bending contribution is proportional to $(h/R)^2$ [36]. For a typical cellular membrane of R = 5 μm and h = 4 nm, h/R is less than 10^{-6} and can thus be neglected. However, strong membrane bending does occur at the contact region. The change from the membrane in contact with the substrate to the free membrane, at the contact angle θ, happens over a length comparable to the membrane thickness. Then the local radius of curvature of the membrane near the separation line can be estimated as ρ =h/θ. Eelastic energy of bending using from beam theory is:

$$G_b \approx \frac{E_m I}{2}\frac{hl}{\rho^2} \quad \textbf{(A10)}$$

where I = h^3/12 is the second momentum of the area of the contact, and l = 4πrsinθ ≈ 4πrθ, is the total length of contact. Substituting l and I back to the expression of the bending energy (Eq. A10), and taking into account the volume conservation requirement $R-R_0 \approx (R_0\,\theta^4)/8$ we obtain:

$$G_b \approx \frac{\sqrt{2}\pi}{3} E_m h^2 R_0 \varepsilon^{3/2} \quad \textbf{(A11)}$$

The force due to contact area bending therefore equals:

$$F_b = -\frac{\partial G_b}{\partial Z} = \frac{\pi}{2\sqrt{2}} E_m h^2 \varepsilon^{1/2} \quad \textbf{(A12)}$$

The ratio between the bending and stretching terms can be calculated using Eq. A9 and Eq. A12:

$$\frac{F_{bending}}{F_{stretching}} \approx \frac{h}{R_0}\frac{1}{\varepsilon^{5/2}} \quad \textbf{(A13)}$$

Given that lipid bilayer thickness (h) is typically 4 nm, while cell radius is above 5 μm, at ε = 0.1-0.3, this ratio is below 0.05. Therefore, one can neglect the bending deformation contribution, and use Eq. A9 to estimate fluid-filled the impermeable spherical membrane's deformation.

Cytoskeletal compression can be estimated using contact Hertz theory. Assuming that glass is much harder than the cell and has infinite radius of curvature, the deformation of the cytoskeleton compressed between two parallel plates can be calculated using [36]

$$F_c = \frac{\sqrt{2}E_c}{3(1-\nu_c^{\,2})} R_0^{\,2} \varepsilon^{3/2} \quad \textbf{(A14)}$$

where R_0 represents the cell contact radius before deformation and E_c and ν_c are the Young's modulus and Poisson ratio of the cytoskeleton, respectively.

Therefore superposition of Eq. A9 and Eq A14 gives overall cell deformation in estimation as:

$$F = \frac{\sqrt{2}E_c}{3(1-\nu_c{}^2)} R_0{}^2 \varepsilon^{3/2} + 2\pi \frac{E_m}{1-\nu} h R_0 \varepsilon^3 \qquad \textbf{(A15)}$$

where first term arises from the cytoskeleton compression resistance and is responsible for global membrane stretching, and membrane-to-cytoskeleton attachment is neglected