Supplementary Material for "Modeling evolution of cell morphology under stretching"

Nanxin Li,[1,2] Xiangtian Kong,[1,2] Xiaoyao Zhang,[1,2] Yuanyuan Cao,[3] Tongsheng Chen,[1,2,4,a)] and Xinlei Li[1,2,5,a)]

[1] *MOE Key Laboratory of Laser Life Science & Institute of Laser Life Science, College of Biophotonics, School of Optoelectronic Science and Engineering, South China Normal University, Guangzhou 510631, China*

[2] *Guangdong Provincial Key Laboratory of Laser Life Science, College of Biophotonics, School of Optoelectronic Science and Engineering, South China Normal University, Guangzhou 510631, China*

[3] *Institute of Nanosurface Science and Engineering (INSE), Shenzhen University, Shenzhen 518060, China*

[4] *SCNU Qingyuan Institute of Science and Technology Innovation Co., Ltd., South China Normal University, Qingyuan 511500, China*

[5] *Guangzhou Key Laboratory of Spectral Analysis and Functional Probes, College of Biophotonics, South China Normal University, Guangzhou 510631, China*

[a)]Authors to whom correspondence should be addressed: chentsh@scnu.edu.cn. xlli@scnu.edu.cn.

1. The calculations of cell membrane stress

When the cell membrane suffers a deformation, the relation between the stress of membrane and the change of membrane area can describe as[1-3]:

$$\Delta S/S_0 = kT\ln(\sigma/\sigma_0)/8\pi k_{\mathrm{b}} + (\sigma - \sigma_0)/K_{\mathrm{a}} \tag{S1}$$

where $\Delta S/S_0$ is the changes of area compared to initial area, k_{b} is the bending modulus of cell, and σ_0 is the initial stress, k is the Boltzmann constant, T is the temperature, K_a is the tensile modulus. The first term represents that the membrane of fluctuations become progressively restricted and the area should increase logarithmically with stress when membrane has a low stress, and the second term represents that the area varies linearly with stress due to direct expansion of area when membrane has a high stress[1].

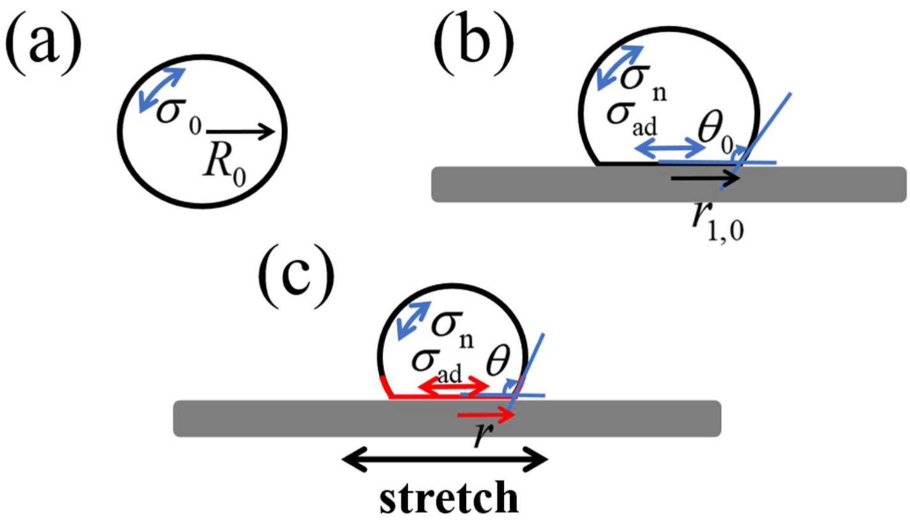

Fig. S1.: (a) The stable morphology of spherical cell with radius of R_0. (b) The stable morphology of adhesion cell on the substrate. (c) The morphology of adhesion cell on the stretched substrate.

When a cell touches the substrate and reaches a stable state, as shown in Fig. S1 (b), the total change of total cell area can be written as:

$$\Delta S = 2\pi r_{1,0}^{\ 2}\left(1+\cos\theta_0\right)/\sin^2\theta_0 + \pi r_{1,0}^{\ 2} - 4\pi R_0^{\ 2} \tag{S2}$$

where the initial cell morphology was considered to be a sphere (radius of R_0, Fig. S1 (a)). The first term represents the area of the non-adhesion membrane, the second term represents the area of the adhesion membrane, and the third term represents the initial area of the cell membrane. If the stresses of the adhesion membrane and non-adhesion membrane are considered to be the same, the stress can be obtained by substituting the change of the cell total area ΔS into Eq. (S1).

In the case of cell adhered on the substrate, the initial area of the adhesion membrane should be the corresponding area in the case of spherical cell which can be calculated as: $S_{\mathrm{ad},0} = 4\pi R_0^{\ 2}\, S_{\mathrm{ad}} / (\mathrm{S}_{\mathrm{ad}} + S_{\mathrm{n}})$ i.e., $S_{\mathrm{ad},0} = \left(4\pi R_0^{\ 2}\right)\pi r_{1,0}^{\ 2} / \left(2\pi r_{1,0}^{\ 2}(1+\cos\theta_0)/\sin^2\theta_0 + \pi r_{1,0}^{\ 2}\right)$. Similarly, the initial area of the non-adhesion membrane can be calculated as: $S_{\mathrm{n},0} = S_0\left(2\pi r_{1,0}^{\ 2}(1+\cos\theta_0)/\sin^2\theta_0\right) / \left(2\pi r_{1,0}^{\ 2}(1+\cos\theta_0)/\sin^2\theta_0 + \pi r_{1,0}^{\ 2}\right)$.

When the substrate suffers a stretching deformation, as shown in Fig. S1 (c), if the adhesion membrane detaches from the substrate, the initial area of the adhesion membrane will decrease and can be calculated as:

$$S_{\mathrm{ad},0}{}' = S_{\mathrm{ad},0}\left(1 - \frac{\pi r_{1,0}^{\ 2}(1+\varepsilon)^2 - \pi r^2}{\pi r_{1,0}^{\ 2}(1+\varepsilon)^2}\right) \tag{S3}$$

According to Eq. (S3), the change of adhesion area relative to initial area can be calculated as:

$$\Delta S_{\mathrm{ad}} = \pi r^2 - S_{\mathrm{ad},0}{}' \tag{S4}$$

By substituting the change of adhesion area ΔS_{ad} and the initial area of the adhesion membrane $S_{\mathrm{ad},0}{}'$ into Eq. (S1), we can obtain the stress of adhesion membrane.

Similarly, due to the detachment of adhesion membrane, the initial area of the adhesion membrane will increase and can be calculated as:

$$S_{\mathrm{n},0}{}' = S_{\mathrm{n},0} + S_{\mathrm{ad},0}\frac{\pi r_{1,0}^{\ 2}(1+\varepsilon)^2 - \pi r^2}{\pi r_{1,0}^{\ 2}(1+\varepsilon)^2} \tag{S5}$$

According to Eq. (S5), the change of non-adhesion membrane area can be calculated as:

$$\Delta S_{\mathrm{n}} = 2\pi r^2 (1+\cos\theta)/\sin^2\theta - S_{\mathrm{n},0}{}' \tag{S6}$$

By substituting the change of non-adhesion membrane area ΔS_{n} and the initial area of the non-adhesion membrane $S_{\mathrm{n},0}{}'$ into Eq. (S1), we can obtain the stress of non-adhesion membrane.

2. The calculation of the change of adhesion radius due to detachment and re-adhesion

During the stretching of the substrate, as shown in the Fig. S2(a), the blue region represents the adhesion area of the cell, and the red region represents the area of reduced adhesion area due to detachment of the adhesion membrane. The reduced length L is determined by the accumulation of detachment of the adhesion membrane between time 0 and t: $L = \int \mathrm{d}L$. In addition to this, this length becomes larger as the substrate stretching occurs (the red region in the Fig. S2(a) increases synchronously as the substrate stretching occurs). Specifically, a time period $(\hat{t}, \hat{t} + \mathrm{d}\hat{t})$ is taken between 0 and t in which the length of radius reduction due to adhesion membrane detachment is $\mathrm{d}l = v(\hat{t})\mathrm{d}\hat{t}$, and this length $\mathrm{d}l$ becomes larger with further substrate stretching. At moment t, the length of $\mathrm{d}l$ is stretched to:

$$\mathrm{d}L = (1+\varepsilon(t))/(1+\varepsilon(\hat{t}))\mathrm{d}l \tag{S7}$$

Overall, the change of radius due to detachment of the adhesion membrane at moment t is:

$$L = -\int_0^t \frac{1+\varepsilon(t)}{1+\varepsilon(\hat{t})} v(\hat{t})\mathrm{d}\hat{t} \tag{S8}$$

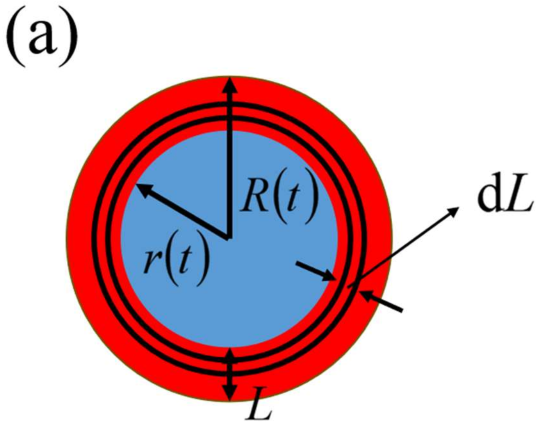

Fig. S2: (a) During the stretching of the substrate, the blue region corresponds to the cell adhesion area, the red region corresponds to the decrease of adhesion area due to detachment of the adhesion membrane, the black line segments are the boundaries corresponding to the taken length $\mathrm{d}L$ and $R(t)$ is the radius of the adhesion membrane at time t during substrate stretching without detachment of the adhesion membrane $R(t)=(1+\varepsilon(t))r_{1,0}$. (b) During the relaxation of the substrate, the blue region corresponds to the adhesion area of the cell without re-adhesion, the red region corresponds to the increase of adhesion area due to cell re-adhesion, the sum of the area of the blue region and the red region is the adhesion area of the cell, the black line segments are the boundaries corresponding to the taken length $\mathrm{d}L'$ and $R'(t)$ is the radius of the adhesion membrane at time t during relaxation of the substrate without cell re-adhesion $R'(t)=(1+\varepsilon'(t))/(1+\varepsilon_0)r_{3,0}$.

Conversely, during the relaxation stage of substrate stretching, the length of cell re-adhesion L' becomes smaller as the relaxation of the substrate occurs. Specifically, a time period $(\hat{t},\hat{t}+\mathrm{d}\hat{t})$ is taken between 0 and t in which the length of radius increase due to cell re-adhesion is $\mathrm{d}l'=v'(\hat{t})\mathrm{d}\hat{t}$, and this length $\mathrm{d}l'$ becomes smaller with further relaxation of the substrate. At moment t, the length of $\mathrm{d}l'$ is relaxed to:

$$\mathrm{d}L'=(1+\varepsilon'(t))/(1+\varepsilon'(\hat{t}))\mathrm{d}l' \tag{S7}$$

Overall, the change of radius due to cell re-adhesion at moment t is:

$$L' = \int_0^t \frac{1+\varepsilon'(t)}{1+\varepsilon'(\hat{t})} v'(\hat{t}) \mathrm{d}\hat{t} \tag{S8}$$

3. The solution of the contact angle of the cells

The contact angle of the cells is variable during cyclic stretching. Solutions to the four-stage equation describing the change of adhesion radius of the cell are provided here (Eq. (5), (7), (12), and (14)). According to $V = \pi r^3 (8 - 9\cos\theta + \cos 3\theta) / 12\sin^3\theta$, Eq. (S1) and Eq. (S3)-(S6), the contact angle of the cell(θ), the cell adhesion membrane stress(σ_{ad}), and the cell non-adhesion membrane stress(σ_{n}) in Eq. (5), (7), (12), and (14) can all be expressed by the adhesion radius(r). So Eq. (5), (7), (12), and (14) can then be viewed as:

$$\mathrm{d}r/\mathrm{d}t = f(r,t) \tag{S9}$$

This is the first order ordinary differential equation for the adhesion radius. We can calculate the instantaneous adhesion radius based only on the initial conditions. According to the instantaneous adhesion radius, we can obtain the instantaneous contact angle. Next, another solution is provided here. Similarly, according to $V = \pi r^3 (8 - 9\cos\theta + \cos 3\theta) / 12\sin^3\theta$, Eq. (S1) and Eq. (S3)-(S6), the adhesion radius(r), the cell adhesion membrane stress(σ_{ad}), and the cell non-adhesion membrane stress(σ_{n}) in Eq. (5), (7), (12), and (14) can all be expressed by the contact angle (θ). Eq. (5), (7), (12), and (14) can then be viewed as:

$$\mathrm{d}\theta/\mathrm{d}t = f(\theta,t) \tag{S10}$$

This is the first order ordinary differential equation for the contact angle. Based on the initial conditions, we can calculate the instantaneous contact angle. According to the instantaneous contact angle, we can obtain the instantaneous adhesion radius. The instantaneous adhesion radius and instantaneous contact angle can describe the morphology change of the cell.

REFERENCES

1. Evans and Rawicz, *Phys. Rev. Lett.*, 1990, **64**, 2094-2097.
2. M. Murrell, L.-L. Pontani, K. Guevorkian, D. Cuvelier, P. Nassoy and C. Sykes, *Biophys. J.*, 2011, **100**, 1400-1409.
3. A. Berthaud, F. Quemeneur, M. Deforet, P. Bassereau, F. Brochard-Wyart and S. Mangenot, *Soft Matter*, 2016, **12**, 1601-1609.