Adhesive Models to Understand the Sensitivity of Bio-Molecules to Environmental Signals

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Abstract: Recently, contact mechanics has been widely used to get some understanding of the biological adhesion mechanisms, such as cell-cell adhesion, insects' adhesion and locomotion. JKR theory is usually adopted as a basis, in which the interaction of molecules is considered in contrast to the classical Hertz solution. In this paper, two problems are summarized, which may give some insights to cells or bio-molecules sensitivity to environmental signals: (1) cell reorientation on a stretched substrate; (2) spontaneous detachment between cells or bio-molecules under the variation of environmental signals. The intention here is only to illustrate the possibilities that contact mechanics may explain or predict some bio-phenomena using simple mechanical models. A complete analysis taking into account the full biological complexities is far beyond the scope of this paper. With this objective in mind, the sensitivity of bio-molecules to the environmental signals is described through the variation of adhesive contact area, which is affected by the external forces or deformations. In the first problem, two-dimensional generalized JKR model is used to explain why there exist three stages with two critical values of stretch amplitude controlling cells' reorientation. Three-dimensional adhesive model is used in the second problem, to analyze the spontaneous detachment between two adhering cells or bio-molecules, which may happen at a critical condition.

Keyword: contact mechanics; biological adhesion mechanism; cell reorientation; bio-molecule; spontaneous detachment

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1 Introduction

Accumulating biological evidences show that cells actively sense and react to mechanical forces and deformations in the environment (Galbraith et al., 1998; Huang and Ingber, 1999; Geiger et al., 2002; Haston et al., 1983; Lo et al., 2000; Lorz et al. 2000; Bischofs and Schwarz 2003; Wong et al., 2003). For example, experiments (as shown Fig. 1) over the last two decades have found that cells cultured on a cyclically stretched substrate tend to reorient themselves away from the stretch direction (Dartsch and Hammerle, 1986; Shirinsky et al., 1989; Kanda and Matsuda, 1993; Neidlinger-Wilke et al., 1994, 2001; Wang et al., 1995; Wang, 2000; Moretti et al., 2004; Dartsch and Betz, 1989; Iba and Sumpio, 1991). An important fact first noted by Dartsch and Hammerle (1986) in the experiment is that cells do not respond to small stretch amplitudes, suggesting that there exists a threshold stretch amplitude to initiate cell reorientation. Above this threshold, cells begin to respond to substrate deformation by reorienting themselves away from the stretch direction. The larger the stretch amplitude, the more cells reorient. Neidlinger-Wilke et al. (1994) reported that almost all cells reorient in a perpendicular direction to the external force once the stretch amplitude exceeds a second threshold level. Wang et al. (1995) and Wang (2000) have shown that, despite of the complex underlying biological responses, the final aligning angle of cells can be predicted based on the principle of minimum strain energy.

At the molecular level, specific binding between protein molecules is believed to play an important role in cell adhesion and signal transduction. Protein molecules are deformable and can alter their conformations under mechanical forces. The
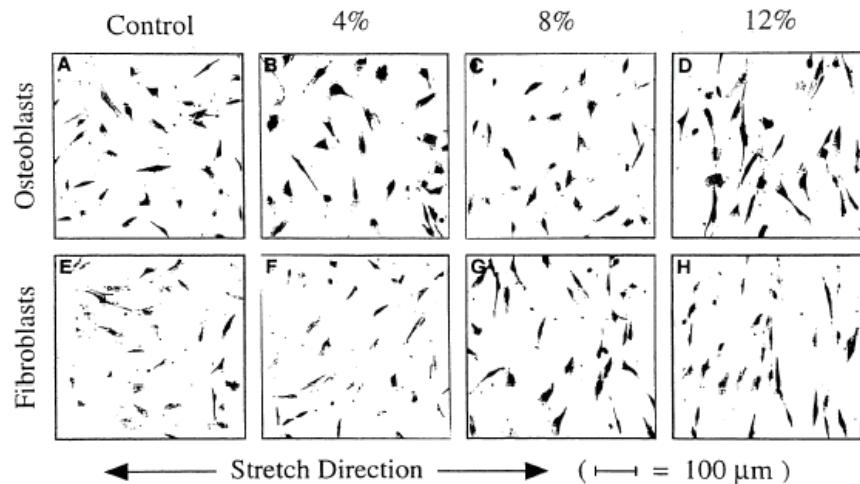
Figure 1: Experiment results of cells cultured on a substrate (Neidlinger-Wilke,et. al 2001), in which cell reorientation can be found and are controlled by the force amplitude.

conformation changes can in turn affect protein-protein and protein-DNA recognition, binding and unbinding (Bao, 2000; Zhu et al., 2000). Bao (2002) discussed that mechanical forces can cause a receptor molecule to deform, thereby altering the conformational match between the receptor and its ligand as shown in Fig. 2. In some cases, the effect of mechanical deformation may decrease the receptor-ligand binding and in others it may enhance the interactions by exposing the binding sites.
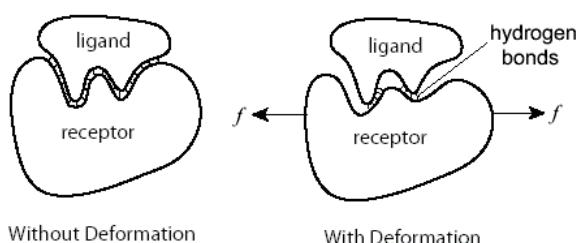
Figure 2: Schematic of the ligand-receptor binding affected by the protein deformation (Bao, 2002). When the receptor is acted an external tension force, bonding between the receptor and the ligand will break due to the receptor's deformation.

Currently, we barely have any theoretical understanding on the above two phenomena. The effort to understand the mechanisms that cells or bio-molecules sense the environmental signals may provide challenging and rewarding opportunities for bio-mechanics in the future.

Inspired by Chu et al. (2005), in which JKR theory was used to explain cells adhesion force, Chen and Gao (2006a, 2006b) and Chen and Gao (2006c, 2007) adopted contact mechanics theories to understand bio-adhesion mechanisms such as cells on stretched substrates and spontaneous detachment of adhering cells or bio-molecules. These studies have significantly expanded the literature on classical adhesive contact mechanics and give some insights to the development of bio-adhesive-mechanics. Due to specific ligand-receptor binding in cell adhesion as well as specific sequence matching in adhesion between bio-molecules, it is assumed that the contact area is perfectly bonded such that both tangential and normal tractions are transmitted across the contact interface, in contrast to the classical JKR model. If there is one to one bonding between specific molecules, shear deformation along the contact interface would not be easily relaxed and shear tractions become so important that interfacial fracture mechanics must be used to describe the elastic field near the contact edge.

In applying simple elastic models to biological phenomena, we caution that the mechanical prop-

erties of cells or proteins can be extremely complex (Howard, 2001; Bao, 2002) and mechanical properties of cells are highly viscoelastic due to the organization of actin cytoskeleton (Howard, 2001). However, contact between viscoelastic bodies is more complicated than the corresponding elastic problems and viscoelastic contact solutions are often history dependent, in which case there is no unique relation between the contact size and the applied load. To avoid excessive complications, we limit our attention to the linear elastic. While these models are far from being realistic with respect to the properties of cells, it provides a limiting solution of a viscoelastic body in response to sufficiently high frequency.

The key ideas and results in our previous work (Chen and Gao, 2006a, 2006c) are summarized in this paper. The reader is encouraged to consult various references given in the paper for more details.

2 Adhesive model for cell reorientation on stretched substrates

In the experiments, the direction of cells cultured on a substrate is initially arbitrary. When the substrate is subjected to a cyclic stretch force, cell will reorient and the degree of reorientation is related to the amplitude of the cyclic force as shown in Fig.2. The whole reorientation process can be divided into three stages by two critical values of the external force amplitude. Why and how does the amplitude of force influence cells' reorientation? De-cohesion is needed for cells to rotate and reorient, new focal adhesions may be formed in a new direction, which will abide the rule of minimum strain energy as demonstrated by Wang (2000). The de-cohesion process can be described by the contact area changes, contact mechanics model may be helpful. As a result, the relation between the contact area and the external stretch force has been studied by Chen and Gao (2006a, 2006b) using a generalized JKR model and a generalized MD model, respectively. Here we only briefly summarize the results of the generalized JKR model (Chen and Gao, 2006a).

Figure 3 is the schematic of the generalized JKR model, in which an elastic cylinder with radius R
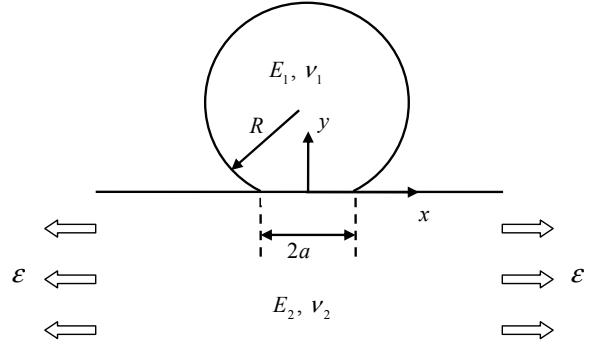
Figure 3: Schematic of an elastic cylinder in adhesive contact with a stretched substrate, where $2a$ denotes the contact width, R is the radius of the above cylinder and ε is the external tension strain acted on the substrate.

adheres to a semi-infinite elastic substrate via intermolecular forces. A uniaxial strain ε is then acted to stretch the substrate to a given strain level. During the stretch of the substrate, the contact region is assumed to be perfectly bonded except that the edge of contact shifts according to the changing balance between elastic energy and surface energy. The edges of the contact region resemble two opposing interfacial cracks under plane strain deformation. Following the JKR model (Johnson et al., 1971), the equilibrium contact area can be determined from the Griffith energy balance between the elastic energy and surface energy.

$$G = \frac{1}{\cosh^2 \pi \kappa} \frac{|K|^2}{2E^*} = \Delta\gamma \tag{1}$$

where $\kappa = \frac{1}{2\pi} \ln \frac{1+\beta}{1-\beta}$ is an oscillation index and β is one of the Dundurs' parameters.

$$\frac{1}{E^*} = \frac{1 - v_1^2}{E_1} + \frac{1 - v_2^2}{E_2} \tag{2}$$

E^* is the effective Young's modulus and E_1, v_1, E_2, v_2 denote Young's moduli and Poisson's ratios of the cylinder and substrate, respectively. $\Delta\gamma$ is the work of adhesion. K is a complex valued stress intensity factor and expressed as

$$K = -\sqrt{2\pi} \lim_{x \to a} (a - x)^r [P(x) + iQ(x)] \tag{3}$$

r is the stress singularity and a the half width of the contact zone. $P(x)$ and $Q(x)$ are normal and tangential tractions on the contact interface. The sign "-" is introduced due to the definition of tractions. Using the continuity condition of displacement across the contact interface and the relation between the surface displacements of an elastic half space and the surface tractions $Q(x)$ and $P(x)$ via Green's functions yields

$$P(x)+iQ(x) = 2iI(x) + \frac{E^*\beta}{2(1-\beta^2)}\left(\varepsilon + \frac{xi}{R}\right) \quad (4)$$

where

$$I(x) = \frac{E^*(a+x)^{-\bar{r}}(a-x)^{-r}}{4\pi(1-\beta^2)}$$
$$\left[\int_{-a}^{a}(-\varepsilon - \frac{ti}{R})\frac{(a+t)^{\bar{r}}(a-t)^{r}}{t-x}dt\right]. \quad (5)$$

and

$$r = \frac{1}{2} + i\kappa \quad (6)$$

One can see that the tractions in Eq. (4) has an oscillatory singularity with an index κ. Combining Eqs. (1), (3) and (4) gives the relation between the contact half-width a and the external tension strain ε. When $\varepsilon = 0$, we denote the contact half-width as a_0. It is found that the ratio of a/a_0 depends on the substrate strain ε only through the parameter λ and $\lambda = R/a_0$.

Figure 4 gives the numerical results of a/a_0 as a function of the substrate strain ε for different values of parameter λ. The result indicates that the behavior of a/a_0 can be characterized by three distinct regimes with two threshold strain levels: (1) the contact width is hardly influenced by the applied loading when the substrate strain is below the first threshold; (2) as the substrate strain increases to between the two threshold values, the contact width begins to decrease significantly in response to the applied loading; (3) the adhesion fails with almost no contact possible when the substrate strain exceeds the second threshold.

Although the above results are derived for the adhesive contact of an elastic cylinder with a stretched substrate, interestingly, the behaviors of the contact area in Fig.4 show several features
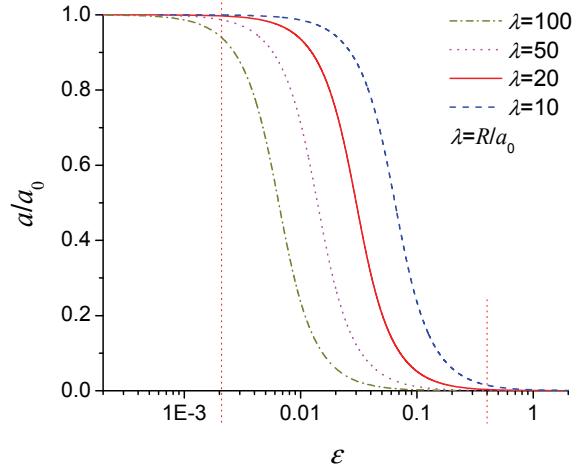
Figure 4: Plot of the contact half-width a/a_0 as a function of the external strain ε for different values of parameter λ, from which one can see three different regimes of the variation of the contact width controlled by two critical values of ε.

which appear to be qualitatively similar to that of cells cultured on a cyclically stretched substrate. Experiments on cell reorientation in response to cyclic substrate stretch also show three characteristic regimes with two threshold stretch amplitudes. It was found that cells do not respond to stretch amplitudes smaller than 1-2% (Dartsch and Hammerle, 1986). Once this first threshold is reached, cells begin to actively reorient themselves away from the stretch. The cell reorientation leads to decreasing contact width in the direction of stretch and increasing contact width in the transverse direction. As the stretch amplitude increases beyond a second threshold level around 5-6%, almost all cells reorient away from the stretch direction (Neidlinger-Wilke et al., 1994). These features and the associated strain levels appear to be in good agreement with our analysis. For the third regime in our analysis, the contact radius becomes quite small and approaching zero with increasing stretch. However, the contact area does not vanish and does not imply full deliminations of cells in this regime. An interpretation of this result is that for large stretch strains cells must fully re-orient to minimize the contact area.

Furthermore, Chen and Gao (2006a) found that

a_0, which is produced only by the intermolecular forces ($\varepsilon = 0$), can be approximated by the corresponding solution a_{JKR} of the classical JKR model, i.e.,

$$a_0 = a_{JKR} = 4 \left(\frac{R^2 \Delta \gamma}{2 \pi E^*} \right)^{1/3}. \tag{7}$$

and the non-oscillatory solution ($\kappa = 0$) can express the relation between a and ε explicitly as

$$\frac{a}{a_0} = \left[\left(\frac{1}{2} + \sqrt{\frac{1}{4} + \frac{64 \lambda^6 \varepsilon^6}{27}} \right)^{1/3} \right.$$
$$\left. - \frac{4 \lambda^2 \varepsilon^2}{3} \left(\frac{1}{2} + \sqrt{\frac{1}{4} + \frac{64 \lambda^6 \varepsilon^6}{27}} \right)^{-1/3} \right] \tag{8}$$

where

$$\lambda = R/a_0 \cong R/a_{JKR} = \left[\frac{\pi R E^*}{32 \Delta \gamma} \right]^{1/3}. \tag{9}$$

In the above non-oscillatory solution, we find that the ratio of a/a_0 depends on the substrate strain ε only through the parameter combination $\lambda \varepsilon$, which is consistent with the oscillatory case. In addition, we find that the relation between a/a_0 and $\lambda \varepsilon$ for the non-oscillatory case matches the oscillatory one very well. In other words, it seems that the oscillatory property may strongly affect the parameters a_0 and λ, but they do not alter the relationship between a/a_0 and $\lambda \varepsilon$. Equation (8) can be a very good approximation to the generalized JKR model shown in Fig.3, so that it is very convenient to predict the contact area using the closed-form solutions in Eqs. (7)-(9).

As we know that the above generalized JKR model produces unphysical singular stress field near the edge of the contact zone. In order to cancel the singularity, the interaction of molecules outside the contact zone should be considered and is often represented by constant normal and tangential tractions, i.e., Dugdale zone. Maugis (1992) studied the three-dimensional case considering constant normal traction outside the contact zone, which is often called Maugis-Dugdale (MD) model. Baney and Hui (1997) developed the Maugis-Dugdale model for adhesion between

elastic cylinders when the shear traction in the contact area is negligible. Extension of the non-slipping JKR model to a generalized Maugis-Dugdale model is to adopt a Dugdale type adhesive interaction law to eliminate the unphysical singular stress field near the edge of the contact zone. Can the result of generalized MD model explain cells' reorientation on stretched substrates? Are there any relations between the results of the generalized JKR and MD models? These questions have been answered by Chen and Gao (2006b), in which it is found that the generalized JKR model gives a rather good qualitative description of both shear and normal tractions in comparison with the physically more realistic Maugis-Dugdale description and the normal traction predicted by the generalized JKR model becomes a good approximation to the corresponding result from the generalized Maugis-Dugdale model as soon as $\tilde{\sigma}_0 > a/R$, where $\tilde{\sigma}_0 = \frac{4 \sigma_0}{\pi E^*}$, σ_0 is the constant normal traction outside the contact zone. Thus, the results derived for non-slipping adhesive contact between an elastic cylinder and a stretched substrate with Dugdale interaction zones outside the contact region also share a number of features with cells' reorientation cultured on a cyclically stretched substrate where experiments show three characteristic regimes with two threshold stretch amplitudes.

3 Adhesive model for spontaneous detachment of bio-molecules

In the above section, we have discussed cells behavior on substrate under external force. Generally, cells or bio-molecules exist in liquid environments, such as blood. If the environmental pressure or temperature changes, how do cells or bio-molecules sense the environmental signals? Does contact mechanics model can explain the sensing process of two adhering cells or bio-molecules? The answer should be very helpful for curing some diseases related to bio-molecules' cluster, such as thrombus. Motivated by these, Chen and Gao (2006c) consider a non-slipping adhesive contact model between two dissimilar elastic bodies subjected to a pair of pulling forces F and a mismatch strain ε_m induced by envi-

ronmental forces such as changes in temperature and/or pressure. The model predicts that the mismatch strain has significant effect on both the contact area and the pull-off process. Under a finite pulling force (which may be interpreted as an effective force due to thermal or entropic forces), a pair of adhering particles is predicted to break apart spontaneously at a critical mismatch strain, thereby suggesting a mechanism by which cells and molecules can detect environmental changes via specific binding interactions.

Three-dimensional generalized JKR model is shown in Fig. 5, in which the contact interface is assumed to be perfectly bonded and the contact edge is allowed to shift according to thermodynamic equilibrium between elastic energy and surface energy. If the shear traction along the contact interface is neglected, as in the classical JKR model, one would predict that the mismatch strain ε_m should have no influence on the contact area. In contrast, this model assumes no slipping along the contact interface so that the contact area will be influenced by both the pulling force F and the mismatch strain ε_m, which has be addressed by Chen and Gao (2006c).

This model has a number of features in common with an external circular interfacial crack, the energy release rate of which can be expressed as the same form as Eq. (1). E^* is the combined Young's modulus with the same form as Eq. (2), E_1, v_1, E_2, v_2 being the Young's moduli and Poisson's ratios of the two contacting spherical objects.

The Griffith energy balance criterion $G = \Delta\gamma$ can be used to describe the relations among the contact radius, the tension force and the mismatch strain ε_m.

The surface displacements and stress components of an elastic half space ($z \geq 0$) subjected to axisymmetric normal and tangential tractions over a circular region of radius a on the surface can be expressed as

$$\begin{cases} u_z(\rho) = & a\int_0^\infty [2(1-v)g(t)-(1-2v)h(t)] \\ & \qquad\qquad\qquad\qquad J_0(\rho t)\mathrm{d}t \\ u_r(\rho) = & a\int_0^\infty [2(1-v)h(t)-(1-2v)g(t)] \\ & \qquad\qquad\qquad\qquad J_1(\rho t)\mathrm{d}t \end{cases},$$
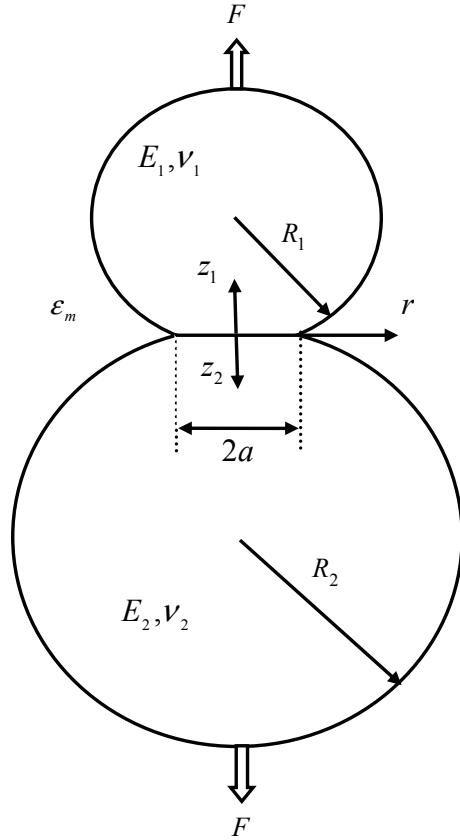
Figure 5: Schematic of two different elastic spheres in perfect adhesive contact under a pair of force F and a mismatch strain ε_m.

$$\tag{10}$$

$$\begin{cases} \sigma_{zz}(\rho) = & -2\mu \int_0^\infty tg(t)J_0(\rho t)\mathrm{d}t \\ \sigma_{rz}(\rho) = & -2\mu \int_0^\infty th(t)J_1(\rho t)\mathrm{d}t \end{cases}. \tag{11}$$

where $\rho = r/a$, $J_0(\rho t)$ and $J_1(\rho t)$ are Bessel functions, the unknown functions $g(t)$ and $h(t)$ correspond to the Hankel transforms of σ_{zz} and σ_{rz}, respectively. μ is Lame's elastic constant of the half space.

The non-slipping conditions on the contact interface of two adhering spheres 1 and 2 are expressed as

$$\Delta u_r = u_{r1} - u_{r2} = \varepsilon_m a\rho$$
$$\Delta u_z = u_{z1} + u_{z2} = \delta - \frac{a^2}{2R}\rho^2 (\rho \leq 1) \tag{12}$$

$$\sigma_{zz1} = \sigma_{zz2} = \sigma_{zz}, \quad \sigma_{rz1} = -\sigma_{rz2} = \sigma_{rz} \tag{13}$$

where R is the combined radius, $1/R = 1/R_1 + 1/R_2$, δ is the relative displacement between the centers of the two objects (Johnson, 1985).

The resultant force in the normal direction of contact interface should satisfy

$$F = 2\pi a^2 \int_0^1 \rho \sigma_{zz}(\rho) \mathrm{d}\rho. \quad (14)$$

Solving the boundary value problem yields the interfacial stress components, which possess oscillatory singularities with an oscillatory index κ. Substituting the interfacial stress components into the Griffith energy release rate G, then using the Griffith energy balance criterion (1), we can write the relation among the contact radius, the tension force and the mismatch strain. However, the governing equation is very complex because of the oscillatory character. Comparing the results of oscillatory ($\kappa \neq 0$) and non-oscillatory ($\kappa = 0$) solutions, Chen and Gao (2006c) find that the effect of β is quite small and can be neglected for practical purposes and the non-oscillatory solutions (with $\kappa = 0$) can serve as an approximate solution to the non-slipping adhesive contact problem between two dissimilar elastic spheres.

The interfacial stresses in the non-oscillatory case are

$$\sigma_{zz}(\rho) = -\frac{2E^* a \sqrt{1-\rho^2}}{\pi R}$$
$$+ \frac{E^*}{\pi} \left[\frac{2a}{3R} + \frac{F}{2E^* a^2} \right] (1-\rho^2)^{-1/2}, \quad (15)$$

$$\sigma_{rz}(\rho) = \frac{-2E^* \varepsilon_m}{\pi} (1-\rho^2)^{-1/2}. \quad (16)$$

which yields the stress intensity factors as

$$K_I = \lim_{\rho \to 1} \sqrt{2\pi a}(1-\rho)^{1/2} \sigma_{zz}(\rho)$$
$$= \frac{2E^* a^{\frac{3}{2}}}{3\sqrt{\pi}R} + \frac{F}{2\sqrt{\pi}a^{\frac{3}{2}}} \quad (17)$$

$$K_{II} = \lim_{\rho \to 1} \sqrt{2\pi a}(1-\rho)^{1/2} \sigma_{rz}(\rho)$$
$$= -2E^* \varepsilon_m \sqrt{\frac{a}{\pi}} \quad (18)$$

Inserting the above two stress intensity factors into the energy balance criterion (1) yields the

pulling force F as a function of the contact radius a and mismatch strain ε_m,

$$\tilde{F} = -\frac{4}{3}\tilde{E}\tilde{a}^3 + \frac{1}{2}\sqrt{32\pi\tilde{E}\tilde{a}^3 - 64\varepsilon_m^2\tilde{E}^2\tilde{a}^4} \quad (19)$$

where

$$\tilde{a} = \frac{a}{R}, \quad \tilde{E} = \frac{E^* R}{\Delta\gamma}, \quad \tilde{F} = \frac{F}{\Delta\gamma R}. \quad (20)$$

Equation (19) describes the relations among the contact radius a, an external tension force F and the mismatch strain ε_m, with the help of which we can analyze the sensing features of two adhering cells or bio-molecules to the variations of environmental signals.

The relation between $\tilde{F}$ and $\tilde{a}$ for three different values of the mismatch strain is plotted in Fig.6, where we take a representative value $\tilde{E} = 10000$. For a given ε_m, the contact radius decreases as the force $\tilde{F}$ changes from compression to tension until the two spheres are pulled off at a critical force. The results in Fig.6 indicate that the mismatch strain has significant effects on the pull-off process and the pull-off force decreases as the mismatch strain increases. There is a one to one relation between the values of mismatch strain ε_m and pull-off force $F_{pull-off}$.
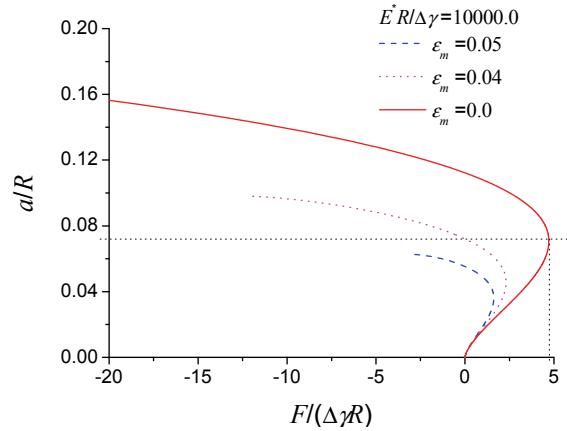
Figure 6: Plot of the contact radius a as a function of the pulling force F for different values of mismatch strain ε_m. The apex of each curves denote the moment of pull-off.

Figure 7 plots the normalized pull-off force $\tilde{F}_{pull-off}$ as a function of the mismatch strain ε_m

for three different values of $\tilde{E}$. In the classical three-dimensional JKR theory, pull-off force is independent of the Young's modulus (i.e., the point of $\varepsilon_m = 0$), but it is no longer true in the presence of a mismatch strain. From Fig.7, it is seen that under a fixed pulling force, there always exists a critical mismatch strain at which a pair of adhering spheres is predicted to break apart spontaneously.
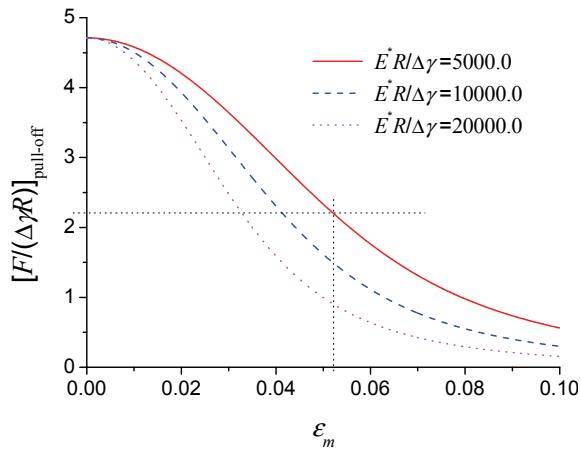
Figure 7: Plot of the relation between the mismatch strain ε_m and the pull-off force $F_{\text{pull-off}}$ for different values of non-dimensional parameter $E^*R/\Delta\gamma$. If the external force F is fixed, there exists a critical value of ε_m, at which two adhering elastic spheres will break apart suddenly.

The generalized three-dimensional JKR model suggests that two adhering objects under thermal fluctuation have an increasing chance to break up in the presence of a mismatch strain induced by environmental signals. The pair of pulling forces acted on the two spheres is analogous to the thermal forces that tend to break apart any adhering particles. Mismatch strains can arise under changes in environmental pressure or temperature or PH values. When the environmental signals (pressure, temperature or PH values) change to some extent and the mismatch strain attains the critical value, adhering particles will break apart spontaneously.

Protein molecules have been adopted as an example to check whether the prediction is reasonable

and feasible by Chen and Gao (2006c). It is found that a mismatch strain on the order of 10% and above would be needed to bring the adhesion energy down to the level of thermal energy K_BT so that the adhering particles would spontaneously dissociate under thermal fluctuation. Conclusions of this three-dimensional model have been further verified by a two-dimensional model in which two different elastic cylinders are in adhesive contact and subjected to a mismatch strain induced by the environmental signals (Chen and Gao, 2007). Experiments are still needed to check the theoretical conclusions.

4 Discussions

The studies discussed in this paper have been aimed at illustrating the applications of contact mechanics to understand some bio-mechanisms, especially for cells' or bio-molecules sensitivity to environmental signals. It is still at a very primitive and premature stage. Much further researches will be needed to understand the biological complexities. As we know that in biological systems, not only mechanics but also chemistry and physiology are important factors for bio-features, behaviors and responses. In the present paper, we only consider the effect of mechanics based on a perfect mechanics model and miss lots of important aspects, such as the time-dependent material behavior (viscoelasticity), focal adhesion between cells and substrates, the organic-inorganic interfaces, the distribution and effect of focal adhesion different from the perfect bonding, the effect of cytoskeleton etc. Numerical simulation is also a helpful method for us to further understand the observations found in bio-experiments.

Why does the first elastic contact mechanics model produce results in qualitative agreement with the mechanical behavior of cells' reorientation which is expected to be strongly viscoelastic? A possible explanation is that the elastic model provides a limiting solution of a viscoelastic body in response to cyclical load at a sufficiently high frequency. In addition, the mechanical response of cells to mechanical forces may be strongly linear (Yang and Saif, 2005). This study shows that it is indeed promising to use mechanics models

to help explain biological behaviors in response to mechanical forces. Thus, bio-experimenters are encouraged to do experiments and verify the theoretical predicted results in the spontaneous detachment model, which can provide useful insights into the basic principles of a complex problem.

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