Supporting Information

Here, we have summarized some of the equations from the several models discussed in the main text. This is supposed to help the reader to quickly look at the resulting equations while reading about a model in the main text, which can clarify the predictions of that model. We urge the reader to refer to the original articles for more detailed explanations or derivations of these equations.

The change in free energy, with three distinct terms for stretching, bending and adhesion energies can be expressed as

$$\Delta F = \frac{1}{2}\kappa_s \frac{(\Delta S)^2}{S_0} + \frac{1}{2}\kappa_b \int_{S_b} (c_1 + c_2 - c_0)^2 \, dS - \gamma \, \Delta S_{ad}$$

Where, and κ_s is the stretching modulus, ΔS and S_0 are the change or increase in membrane area due to stretching and the original area, respectively. κ_b is the bending modulus; c_1 and c_2 are the largest and smallest curvatures, i.e., the principal curvatures at a point in the membrane and c_0 is the spontaneous curvature, which is the natural tendency of the membrane to bend as a result of possible material asymmetries between its two faces. This can be taken to be zero assuming symmetrical membranes. S_b is the area of the membrane bent around the pillar surface**.** γ is the specific adhesion strength per unit area, ΔS_{ad} is the membrane area adhered to the nanopillars. This equation was used by Li and Xiao *et al*. in their models.[1-3]

Pogodin *et al*. derived the following equation to calculate change in free energy and relate it to strain in the membrane [4]

$$F = \int_A \frac{\zeta k \, dS}{1 + \alpha(r)} + \int_{A+B} \frac{k}{2}\alpha^2(r) \frac{dS}{1 + \alpha(r)} + \lambda k \left(\int_{A+B} \frac{dS}{1 + \alpha(r)} - S_0 \right)$$

Where $\alpha(r)$ is the stretching degree at a point, k is the stretching modulus, and ζ is the interaction parameter and λ is the Lagrange multiplier. Note that these terms do not have a different physical meaning, but simply are expressed differently mathematically because of how the author defined the physics behind the process.

Zahir *et al*. used the following equation [5]

$$F = k\int \frac{k^2\lambda^2 - (2\lambda+1)k\varepsilon'(y) + \varepsilon'(y)^2}{[k(1+\lambda) - \varepsilon'(y)]^2}\, dS$$

subject to the constraint,

$$S_0 = \int \frac{k^2}{[k(1+\lambda) - \varepsilon'(y)]^2}\, dS$$

$\varepsilon^{'}$ is the effective adhesion energy that includes contributions of both stretching and bending energy.

Xue *et al*. derived the following equations in their study to evaluate wall tension resulting from gravity.[6]

For nanoridges,

$$\alpha_A = \frac{\lambda R^2}{2\gamma E_M H}\left[\frac{D}{2r_0}\left\{1+\left(\frac{2Hr_0}{R^2}\right)^2\right\}^{\frac{1}{2}} - \left\{1+\left(\frac{2Hr}{R^2}\right)^2\right\}^{\frac{1}{2}}\right]$$

$$\alpha_B = \frac{\lambda R^2(D-2r_0)}{4\gamma E_M H r_0}\left(1+\left(\frac{2Hr_0(2r-D)}{R^2(2r_0-D)}\right)^2\right)^{\frac{1}{2}}$$

Where, α_A and α_B are the stretching degrees for the regions adhered to the pillars and suspended between them, respectively. r_0 can be found using the constraint,

$$S_0 = \int_0^{r_0} \left[\frac{1 + \left(H\left(1 - \frac{2r}{R^2}\right)\right)^2}{1 + \alpha_A} \right]^{\frac{1}{2}} dr + \int_{r_0}^{D/2} \left[\frac{1 + \left(\frac{2Hr_0}{R^2}\left(\frac{r - \frac{D}{2}}{\frac{D}{2} - r_0} \right)\right)^2}{1 + \alpha_B} \right]^{\frac{1}{2}} dr$$

For nanopillars,

$$\alpha_A = \frac{\lambda R^2}{4\gamma E_M H}\left(\frac{D^2}{\pi r_0^2} - 1\right)\left(1 + \left(\frac{2Hr_0}{R^2}\right)^2\right)^{\frac{1}{2}} + \frac{2Hr^2}{3R^2\gamma E_M}\left(\frac{r_0^3}{r^3} - 1\right)$$

$$\alpha_B = \frac{\lambda R^2}{4\gamma E_M H}\left(\frac{D^2}{\pi r_0^2} - 1\right)\left(1 + \left(\frac{2Hr_0}{R^2}\right)^2\right)^{\frac{1}{2}}$$

Subject to the constraint,

$$S_0 = \int_A \frac{8\pi Hr^2/3R^2}{1 + \alpha_A} dr + \frac{2\left(1 - \cos\theta_0\right)\left(D^2 - \pi r_0^2\right)}{\sin^2\theta_0 (1 + \alpha_B)}$$

Watson *et al*. defined two possible scenarios [7]

If the change in surface energy is comparable to the cost of bending and stretching, i.e. in the slow-binding scenario,

$$T.S = \frac{\pi\gamma}{nT} - \frac{\pi E_M T^2}{24\, nR^2}$$

Where, $T.S$ is the tensile strength of the cell wall, T is its thickness, R is the radius of the pillar, E_M is the Young's modulus, γ is the surface energy, and n is the number of neighboring pillars.

If the change in surface energy is far greater than the cost of bending and stretching, i.e. in the fast-binding scenario,

$$T.S = E_M\left[\frac{1.1R + 2h_{max}}{D + 2R}\right]$$

Where h_{max} can be found by solving the quadratic equation,

$$\left[\frac{2E_M nRT}{D + 2R}\right]h_{max}^2 + \left[\frac{2.2E_M nTR^2}{D + 2R} + \frac{\pi E_M T^3}{12R} - 2\pi\gamma R\right]h_{max} + \left[\frac{0.6BnTR^3}{D + 2R} + \frac{\pi E_M T^3}{12} - 2\pi\gamma R^2\right] = 0$$

Where, D is the pillar interspacing.

Valiei *et al*. derived the following equation by assuming ideal cylindrical cell geometry (as shown in fig 5B) and solving the integral given in the main text.[8] The force acts along the pillar height.

$F_c = 2\gamma(\pi R \sin\alpha + L)\sin(\alpha + \theta)\ ; 0 \leq \alpha \leq \pi$

where L is the length of the cylindrical part of the bacterium, R is the radius of the hemispherical edge of the bacterium, θ is the contact angle of the liquid with the bacterial surface, and α is the falling angle describing the position of three-phase contact line on the hemispherical end of a bacterium.

Table S1: Values of different parameters used in various studies discussed in the text.

Author; Year		Parameter	Value	Ref
Li; 2016		Stretching modulus	1 mN/m or 0.25 k_BT /nm^2	2
		Bending modulus	10 k_BT	
		Specific adhesion strength	10 mJ/nm^2 or 0.2 k_BT /nm^2	
	E. coli	Radius of cell	200 nm	
		Length of cell	2 µm	
Xue; 2015		Cell density	10^3 kg/m^3	6
		Diameter	0.2-7 um	
		Gravitational force experienced	2-70 mN/m^2	
		Bond energy of peptide bond	362.3 kJ/mol	

		Critical stretching degree (required to rupture the wall)	0.11	
		Mechanical strength of one peptidoglycan monomer, per unit area	1.145 N/m^2	
		Elastic modulus	10.528 Pa	
	Gram-positive	Cell wall thickness	≈ 30.9 nm	
	Gram-negative	Cell wall thickness	≈ 3.6 nm	
Xiao; 2020	*S. aureus*	Size	0.74 ± 0.11 μm	3
		Thickness	15 – 30 nm	
		Area compressibility modulus	1.25 k_BT /nm^2	
		Bending elastic modulus	100 k_BT	
		Specific adhesion strength	0.25 k_BT /nm^2	
Li; 2016		Stretching modulus	1 mN/m or 0.25 k_BT /nm^2	1
		Bending modulus	10 k_BT	
		Specific adhesion strength	5 mJ/nm^2 or 0.1 k_BT /nm^2	
	S. aureus	Radius of the cell	1 μm	
Liu; 2019	Hertz model	Poisson's ratio	0.5	9
	Creep deformation	Exponent for time (m)	1	
		A	6.8 * 10^{-10}	
		n	1.98	
		Elastic strength of cell wall	1 MPa	
Mirzaali, 2018	*S. aureus* (Cell wall)	Elastic modulus	6 kPa	10
		Poisson's ratio	0.278	

	S. aureus (Cytoplasm)			
	Neo-Hookean hyper elastic properties	C_0	6.21 * 10^5 MPa	
		D	1666.7 MPa^{-1}	
	Viscoelastic properties (Prony series)	Prony coefficient (g_1)	0.39	
		k_1	0	
		τ	187.5 s	
	S. aureus	Mass	1 pg.	
Velic´, 2019	*B. subtilis*	Elastic modulus	115 MPa	[11]
		Poisson's ratio	0.118	
		Interaction forces	100 pN/pillar	

k_B is the Boltzmann constant, T is the temperature.

For typical phospholipid bilayers, $\kappa \approx 20\ k_BT$, where $k_BT \approx 4.1 \times 10^{-21} J \approx 0.6\ kcal\ mol^{-1}$ is the thermal energy.

Table S2: Current reports on modelling of bactericidal actions of nanopatterned surfaces

Year	Brief description	Driving force	Ref.
2013	Adsorption of the cell wall to the nanopillar surface is spontaneous causes the wall to stretch in the region suspended between nanopillars, which finally leads to rupture when the stretching degree exceeds the elastic strength of the membrane.	A decrease in overall free energy	[4]
2015	Gravity induced tension in the cell wall causes stretching and finally causes mechanical failure and rupture at the tip of the adsorbed region.	Gravitational pull	[6]
2016	Stretching of the cell wall of bacteria resting on a nanopillar surface occurs until equilibrium is reached, which is decided	A decrease in overall free	[1]

	by a balance between adhesion free energy and the stretching as well as bending free energies.	energy	
2016	Stretching of the cell wall of bacteria resting on a nanopillar surface occurs until equilibrium is reached, which is decided by a balance between adhesion free energy and the stretching as well as bending free energies.	A decrease in overall free energy	[2]
2018	Stresses generated at the pillar tip due to the body force acting on a bacterial cell as a result of gravitational pull and the weight of the water column above it are responsible for excessive stretching at rupture at the tip.	Pressure due to water column above cell	[10]
2019	Decreasing interfacial energy gradient along the pillar surface creates a pressure on the cell and pulls it down along the pillar surface.	Interfacial energy gradient	[9]
2019	The decrease in surface energy due to the attraction of the cell wall to the nanopillar surface provides the work needed to stretch the bacterial cell wall between the nanopillars.	A decrease in overall surface energy	[7]
2019	Cohesive interactions between bacteria and pillars pull the cell downwards and generate strains at the pillar tip, ultimately causing it to rupture.	Bacteria-pillar cohesive interactions	[11]
2020	Spontaneous adsorption of the cell wall to nanopillar surfaces compensates for the energy required for bending and stretching and causes stretching of the cell wall in the region suspended between pillars.	A decrease in overall free energy	[5]
2020	Stretching of cell wall resting on a nanopillared surface occurs until equilibrium is reached, which is decided by a balance between adhesion free energy and stretching and bending free energies.	A decrease in Gibbs free energy	[3]
2020	The force resulting from the gravitational pull on the cell causes pillars to penetrate and rupture it.	Gravitational pull	[12]

Table S3: Several interesting experimental findings refute current understanding or present other relevant scenarios where current models do not apply.

Year	Brief description	Techniques used	Ref.
2017	Initially, the cell gets in contact with and firmly adheres to a few relatively taller pillars through EPS secretion. Then, as it tries to move away from the jagged topography, the shear forces created cause the inner and outer membrane to separate, eventually leading to rupture and leaking of intracellular fluid.	HIM, FIB-SEM, TEM tomography	[13]
2018	Cells resting on very high aspect ratio CNTs cause them to buckle, bend, and store elastic strain energy, which can provide activation energy for rupturing the wall when high enough.	FIB-SEM	[14]
2020	Cells on nanopillars seldom get penetrated and ruptured by the HARNs. Deformation and stretching induced by the nanostructures cause a high-stress environment and activate intracellular machinery in response, leading to excessive ROS generation. This ultimately leads to death.	SEM, TEM, 3D reconstructions of TEM images, Protein screening	[15]
2020	Cells on nanopillars are generally viable and only get killed when an air-liquid interface passes through them and exerts high downward forces due to capillary forces in the process.	Fluorescence microscopy, SEM	[8]
2020	When cells are tall enough, bacteria resting on top of them pull and bend them and store elastic strain energy in the process. This can provide enough activation energy to cause rupture later.	FIB-SEM	[16]

Table S4: List of symbols frequently used in equations in this article

Symbol	Description	Unit

κ_a	Stretching or compressibility modulus	N/m or k_BT/nm^2
κ_b	Bending modulus	k_BT
γ	Specific adhesion strength per unit area	k_BT/nm^2
ΔF	Change in free energy	k_BT
F	Free energy	k_BT
S_0	Original surface area	m^2
ΔS	Change in surface area	m^2
S	Final surface area	m^2
R	Radius of pillars	nm
H	Height of pillars	nm
D	Interspacing of pillars	nm
h	Drop height	nm
E_M	Young's modulus	Pa

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