ME 470: Mechanics of Soft and biological matter.

LECTURE 12: ADHESION OF MEMBRANES

CONTENTS

- CELL-SUBSTRATE ADHESION
- CELL-CELL ADHESION.

5. ADHESION OF MEMBRANES

5.1. MOTIVATION.

HOW DO CELL COLLECTIVES MAINTAIN THEIR STRUCTURAL INTEGRITY?

$\Rightarrow$ THERE EXISTS ADHESION BY MOLECULAR BOND.

CELL-SUBSTRATE: e.g. INTEGRINS, ORGANIZED IN FOCAL ADHESION

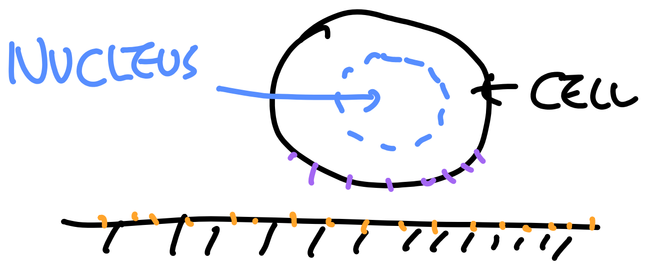
CELL-CELL: e.g. CADHERINS, ORGANIZED IN DESMOSOMES

$\Rightarrow$ DESCRIBE AS $\dfrac{\text{ADHESION ENERGY}}{\text{AREA}} \equiv W$

- TYPICAL BOND ENERGIES OF ADHESION MOLECULES: $\sim k_B T \cdots 35 k_B T$
- TYPICAL ADHESION ENERGY $\longrightarrow$ $W \sim 10^{-5}\ J/m^2$

$\Rightarrow$ MOLECULE DENSITY $n \sim 5 \times 10^{16}\ 1/m^2$

5.2. CONTACT LINES & ADHESION.



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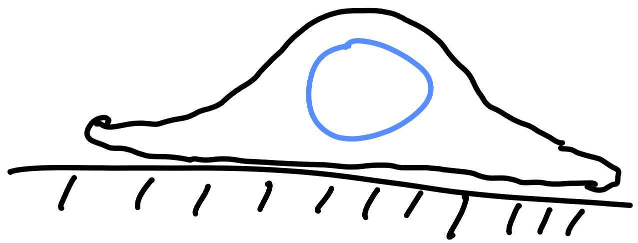
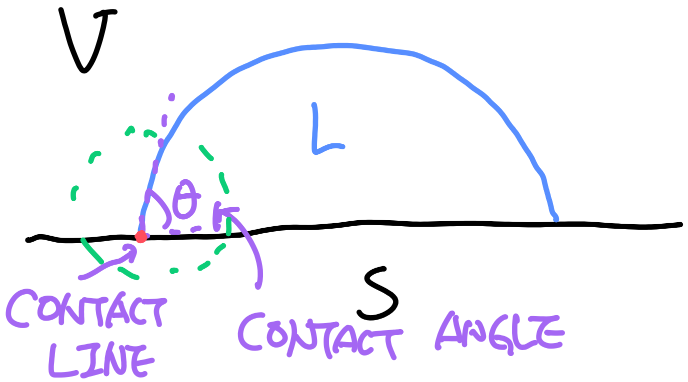
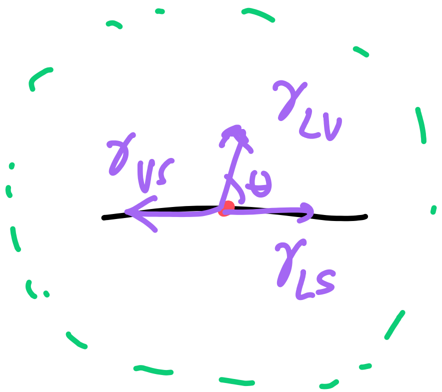


ANALOGOUS TO DROPLET SPREADING?





$$\gamma_{VS} = \gamma_{LS} + \gamma_{LV} \cos\theta$$

$$\Rightarrow \cos\theta = \frac{\gamma_{VS} - \gamma_{LS}}{\gamma_{LV}}$$

(YOUNG'S EQN)

ALTERNATIVELY, MINIMIZE ENERGY

$$E_{TOT} = \gamma_{LV} \cdot A_{CURVED} + \gamma_{LS} \cdot A_{flat} + \gamma_{VS} (A_0 - A_{flat})$$

← CONSTANT.

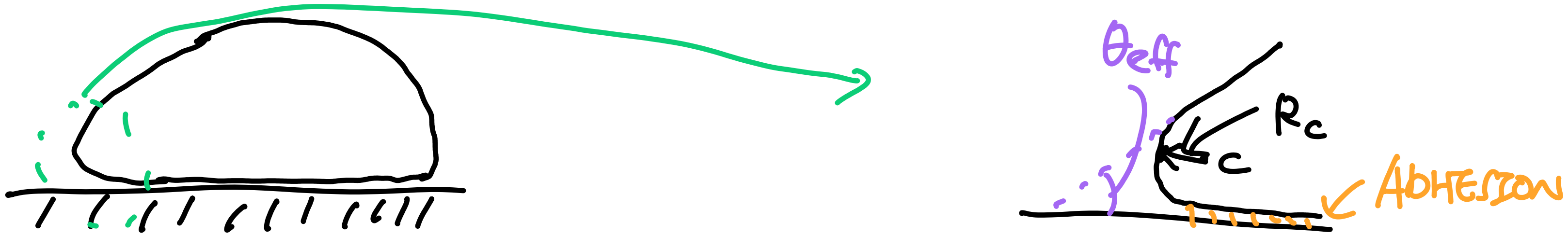
$$dE_{TOT} = \gamma_{LV} A_c + (\gamma_{LS} - \gamma_{VS})\, dA_f$$

USE GEOMETRY. $\dfrac{dA_c}{dA_f} = \cos\theta$, $dE_{TOT} = 0 \Rightarrow \gamma_{LV} \cdot \cos\theta = \gamma_{VS} - \gamma_{LS}$ ✓

6.3. MEMBRANE - SUBSTRATE ADHESION.

DROPLET PICTURE HAS DIVERGENT H @ CONTACT LINE

$\Rightarrow$ DIVERGENT U_{bend}



SIMPLE ENERGY BALANCE:

$$U_{bend} + U_{adh} = U_{TOT}$$

$$\Rightarrow \frac{1}{2}K_b\left[2\cdot\frac{1}{2}\left(\frac{1}{R_c}+0\right)\right]^2\cdot R_c\cdot(\pi-\theta_{eff}) + (-W)\left[\overset{\text{CONSTANT.}}{L_0} - R_c(\pi-\theta_{eff})\right] = U_{TOT}$$

$$\Rightarrow \delta U_{TOT} = \left[\frac{1}{2}K_b\cdot\left(\frac{-1}{R_c^2}\right)\cdot dR_c + W\,dR_c\right]\cdot(\pi-\theta_{eff}) \overset{!}{=} 0$$

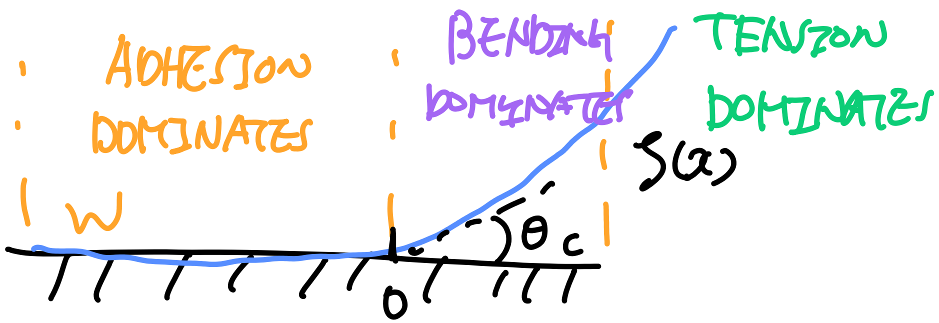
$$\Rightarrow \boxed{W = \frac{k_b}{2R_c^2}} \quad \text{OR} \quad \boxed{R_c = \sqrt{\frac{k_b}{2W}}}$$

ESTIMATE, ASSUMING ONLY LOCAL CHANGE OF GEOMETRY (NEAR CONTACT LINE), BUT, GENERALLY VALID IN 2D AND 3D OBJECTS [SEIFERT & LIPOWSKY, PRA, 1990, 1991]

WHAT IF THERE IS ALSO A TENSION τ IN MEMBRANE?

$$U_{tot} = \frac{1}{2} k_b \int (2H)^2 dA + \tau \int dA - W \int_{flat} dA$$

LOCAL MODEL [SIMSON ET AL. BIOPHYS. JR. 1998]



$$U_{tot} = \frac{1}{2}K_b \int_0^\infty \zeta''(x)^2\, dx - W\int_{-\infty}^0 dx + \tau\int_{-\infty}^0 dx + \tau\int_0^{-\infty} \sqrt{1+\zeta'(x)^2}\, dx$$

EXPAND.

$$\Rightarrow 1+\frac{1}{2}\zeta'(x)^2$$

$$= \int_0^\infty \left(\frac{1}{2}K_b\zeta''(x)^2 + \frac{1}{2}\tau\zeta'(x)^2\right)dx \underbrace{- W\int_{-\infty}^0 dx + \tau\int_{-\infty}^{\infty} dx}_{\text{CONSTANT}}$$

VARIATION $\Rightarrow$

$$-\frac{d}{dx}\cdot\left(\tau\zeta'(x)\right) + \frac{d^2}{dx^2}\left(K_b\zeta''(x)\right) = 0 \Leftrightarrow \frac{K_b}{\tau}\cdot\zeta^{(4)} - \zeta'' = 0$$

$$\Rightarrow \zeta(x) = Ae^{x/\ell} + Be^{-x/\ell} + Cx + D \qquad (\ell^2 \equiv K_b/\tau)$$

REGULARITY: $A=0$ $\qquad \zeta(0)=0 \Rightarrow B=-D$

AND $\zeta(x) = (\tan\theta_c)x$ AS $x\to\infty \Rightarrow C = \tan\theta_c$

AND

$$\zeta''(x=0) = \frac{B}{\ell^2}e^{-x/\ell}\Big|_{x=0} = \frac{1}{R_c} = \sqrt{\frac{2W}{K_b}} \Rightarrow B = \ell^2\cdot\sqrt{\frac{2W}{K_b}} = \sqrt{2WK_b/\tau^2}$$

BALANCE ADHESION $\Leftrightarrow$ CURVATURE

$$\Rightarrow \quad \zeta(x) = (\tan\theta_c)\, x + \sqrt{\frac{2Wk_b}{\tau^2}} \cdot \left(e^{-x\alpha} - 1\right)$$

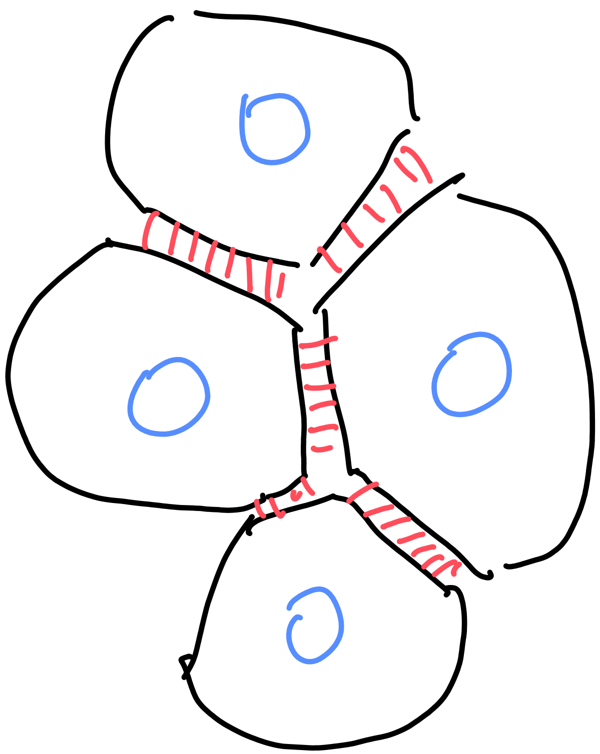
AND USE $\zeta'(x=0)=0$ (MEET SUBSTRATE @ π):

$$(\tan\theta_c) \stackrel{!}{=} \sqrt{\frac{2W}{\tau}}$$

$$\boxed{\zeta(x) = \sqrt{\frac{2W}{\tau}}\, x + \sqrt{\frac{2Wk_b}{\tau^2}} \left(e^{-\sqrt{\tau/k_b}\cdot x} - 1\right)}$$

MAYBE, PLOT THIS IN MATHEMATICA?

6.4. CELL-CELL ADHESION



6.4.1. DIFFERENTIAL ADHESION HYPOTHESIS (DAH)

ALSO, GENERALIZED AS DIFFERENTIAL INTERFACIAL TENSION HYPOTHESIS

CONSIDER CELL TYPE A, B: MODEL AS DROPLETS WITH UNIFORM SURFACE TENSION, γ AND SPECIFIC SURFACE TENSIONS

$$\gamma_{AA} = \gamma - W_{AA}$$

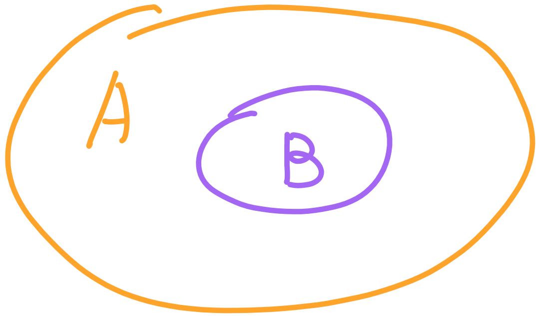
$$\gamma_{AB} = \gamma - W_{AB}$$

$$\gamma_{BB} = \gamma - W_{BB}$$

ADHESION STRENGTH SUCH THAT

$$W_{AA} > W_{AB} > W_{BB}$$

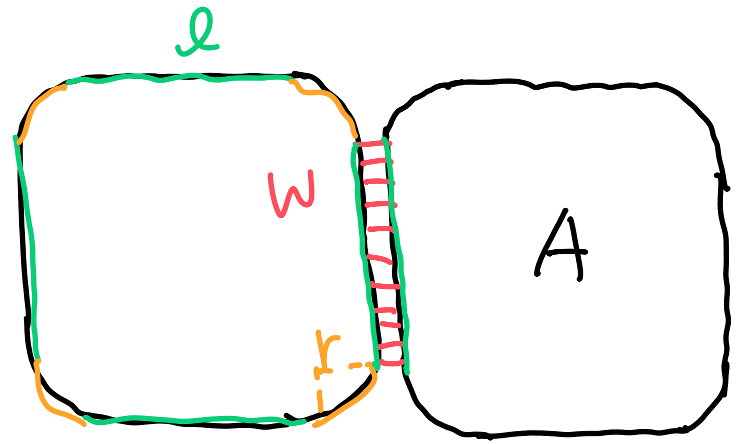
$\Rightarrow$ TISSUE SEGREGATION.



[DAH: STEINBERG, J EXPTL. ZOOL. 1970,

FORTY, & STEINBERG, INT J. DEV. BIOL. 2004]

6.4.2. COMPETITION BETWEEN ADHESION & BENDING



SIMPLE MODEL:

(2D. UNIFORM IN $\hat{z}$)

ASSUME THAT THERE IS NO VOLUME CHANGE

$$\Rightarrow A = \text{CONSTANT} = l^2 + 4rl + \pi r^2$$

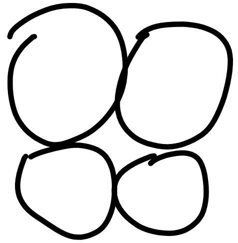
PER CELL

$$\Rightarrow r = \frac{1}{\pi}\left(-2l + \sqrt{(4-\pi)l^2 + A\pi}\right) = r(l)$$

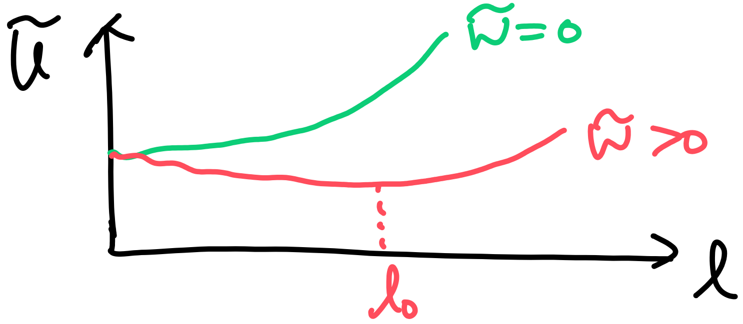
$$U_{TOT} = \underbrace{\frac{1}{2}K_b \cdot \frac{1}{r^2} \cdot 2\pi r}_{U_b} - W \cdot 4l \cdot \frac{1}{2}$$

$$\tilde{U} = \frac{U_{TOT}}{K_b} = \frac{\pi}{r(l)} - 2\tilde{W}l \qquad \left(\tilde{W} \equiv \frac{W}{K_b}\right)$$

$w=0$ EXPECT, $l=0$



Q: IS THERE A CRITICAL ADHESION $\tilde{w}$ FOR FINITE ATTACHMENT?



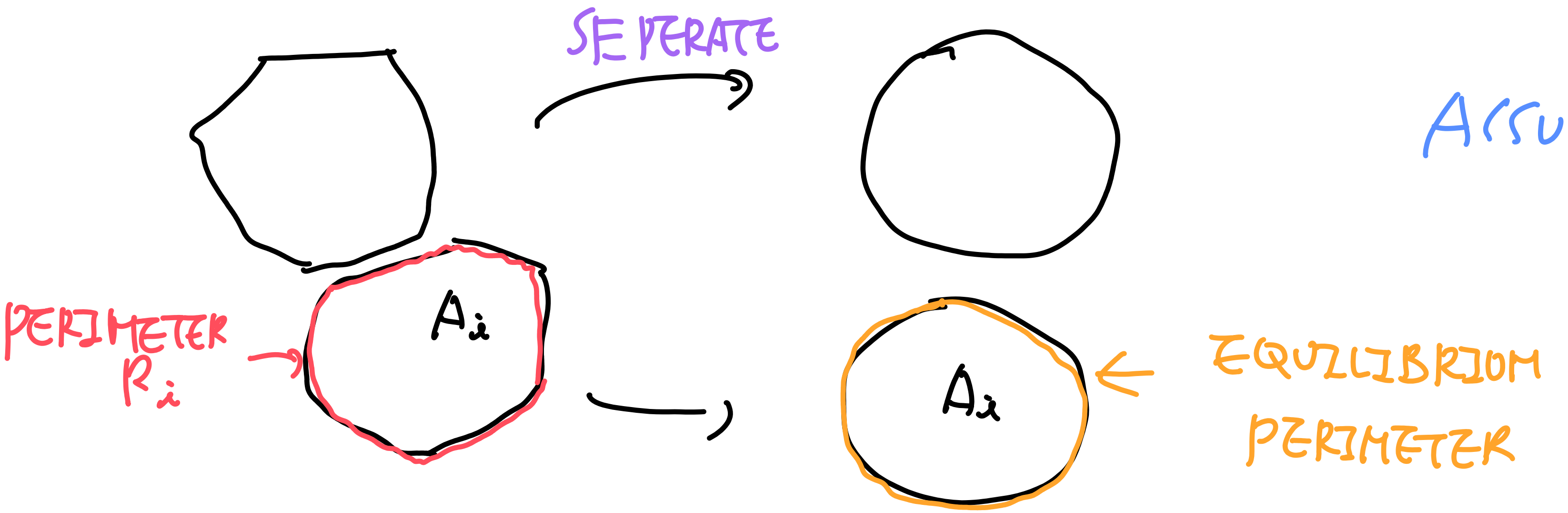
$\Rightarrow$ TO HAVE FINITE l, AT EQUILIBRIUM, WE NEED A CONDITION S.T.

$$\left.\frac{d\tilde{u}}{dl}\right|_{l=0} < 0 \quad , \quad \frac{d\tilde{u}}{dl} = \frac{-\pi}{r(l)^2}\cdot\frac{dr}{dl} - 2\tilde{w}$$

$$\frac{dr}{dl} = \frac{1}{\pi}\left(-2 + \frac{(4-\pi)l}{\sqrt{(4-\pi)l^2 + A\pi}}\right) \Rightarrow \left.\frac{dr}{dl}\right|_{l=0} = \frac{-2}{\pi} \quad , \quad r^2(0) = \frac{A}{\pi}$$

$$\left.\frac{d\tilde{u}}{dl}\right|_{l=0} = -\frac{\pi^2}{A}\cdot\left(\frac{-2}{\pi}\right) - 2\tilde{w} = 0 \Rightarrow \boxed{\tilde{w} = \frac{\pi}{A} \, . \quad w = \frac{\pi}{A}k_b}$$

6.4.3. COMPETITION BETWEEN ADHESION, & STRETCHING.



ASSUME 2D.

$P_{0,i} = 2\sqrt{\pi A_i}$

$$U_{STRETCH,i} = \underbrace{\frac{1}{2} K_A \frac{(P_i - P_{i,0})^2}{P_{i,0}}}_{\frac{1}{2} K_A \int \varepsilon_{ll}^2 \, dl} \quad , \quad U_{adh,i} = -\frac{1}{2} W \cdot P_i$$

ASSUME PERFECTLY CONFLUENT SYSTEM

$\Rightarrow$ MINIMIZE ENERGY TO GET TISSUE EQUILIBRIUM STRUCTURES

$\Rightarrow$ CAN ALSO ADD A BENDING ENERGY TERM.

$$U_{b,ij} = \frac{1}{2} K_b \, C_{ij}^2 \cdot L_{ij} \quad \left(\text{BETWEEN CELL } i \text{ AND } j\right) \quad K_b \simeq \frac{1}{12} K_A \cdot h^2$$

6.5. EMERGENT PROPERTIES OF BIOLOGICAL TISSUES.

BIOLOGICAL TISSUES ARE MAINLY COMPOSED OF CONSTITUENT CELLS.

⇒ INTERACTIONS BETWEEN CELLS DETERMINES EMERGENT PROPERTIES OF TISSUES.

BUT, TISSUES INCLUDE A LARGE NUMBER OF CELLS SO ANALYTIC APPROACHES HAVE A LIMITATION.

⇒ NUMERICAL CALCULATION.

① DISCRETIZE CELLS AND IMPLEMENT INTERACTIONS

② EXPLORE DIFFERENT CELLULAR PROPERTISE, AND THEIR ROLE

IN TISSUE MECHANICS

$\Rightarrow$ INTRODUCE DIFFERENT MODELLING APPROACH.