Updated: Jun 15 2021

FOR ONE CELL

$F_p = (F + \Delta F)e^{-T/(T_0+T)} - \xi V$ is the protrusive force at the cell front.

- $(F + \Delta F)$ is the maximal adhesion/protrusion force
- Exponential term reflects the breaking off cell-substrate adhesions due to tension
- Protrusion decreases as speed increases (assume linear proportionality)

$F_r = (F - \Delta F)e^{-T/(T_0-T)} + \xi V$ is the retraction force at the cell rear.

Assumptions (from linear approximation): $e^{-T/(T_0+T)} \approx 1 - \dfrac{T}{T_0 + T}$ and $\Delta F \ll F$ and $T \ll T_0$

Non-dimensionalization:

$t = T/F, t_0 = T_0/F, f = \Delta F/F \ll 1, \tau = T/F \ll 1$, and $v = F/\xi$. Then:

Front: $(1+f)\left(1 - \dfrac{t}{t_0 + \tau}\right) - v = t\cos\theta$ (1)

Rear: $(1-f)\left(1 - \dfrac{t}{t_0 - \tau}\right) + v = t\cos\theta$ (2)

Subtracting Eq. (1) from Eq. (2), we obtain:

$$2v = 2f - tf\left(\frac{1}{t_0 - \tau} + \frac{1}{t_0 + \tau}\right) + t\left(\frac{1}{t_0 - \tau} + \frac{1}{t_0 + \tau}\right)$$

Getting rid of second-order smaller terms, we have:

$$v \approx f + \frac{t}{t_0}\left(\frac{\tau}{t_0} - f\right)$$

Adding Eq. (1) and Eq. (2):

$$\cos\theta \approx \frac{1}{t} - \frac{1}{t_0} \approx \frac{1}{t}$$ since t_0 has to be greater than t

To find the radius we use the area $A = \pi R^2 \dfrac{\theta}{\pi} - 2\,\dfrac{1}{2} R^2 \cos\theta \sin\theta$, and find the non-dimensional radius is

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$$r = \frac{R}{\sqrt{A}} = \left(\theta - \frac{1}{2}\sin(2\theta)\right)^{-1/2}$$

The non-dimensional pressure differential is $p = t/r$

<u>FOR TWO CELLS (numerics)</u>

Let **index 1 denote leader cell** while **index 2 denotes trailer cell**.

Hmm… choice of parameters to get this going.

“Knowns”: f, t1, t2, t0, tau, tcc, xi (drag or constant of proportionality in Step 9)

Symbol		Meaning (non-dimensional quantities)
f	$\frac{\Delta F}{F}$	Maximal adhesion/protrusion
t_1	$\frac{T_1}{F}$	Leader membrane tension
t_2	$\frac{T_2}{F}$	Trailer membrane tension
t_{cc}	$\frac{T_{cc}}{F}$	Cell-cell adhesive forces
t_0	$\frac{T_0}{F}$	Characteristic tension that breaks cell-substrate adhesion
τ	$\frac{T}{F}$	Ratio of membrane tension to adhesion/protrusion
ξ	Effective viscous drag	Effective viscous drag

** Start with a guess for $w = -1.0$ (the angle between the cell-cell interface and a vertical line).

** Start with a guess for $v = f + t_1\left(\frac{\tau}{t_0^2} - \frac{f}{t_0}\right)$.

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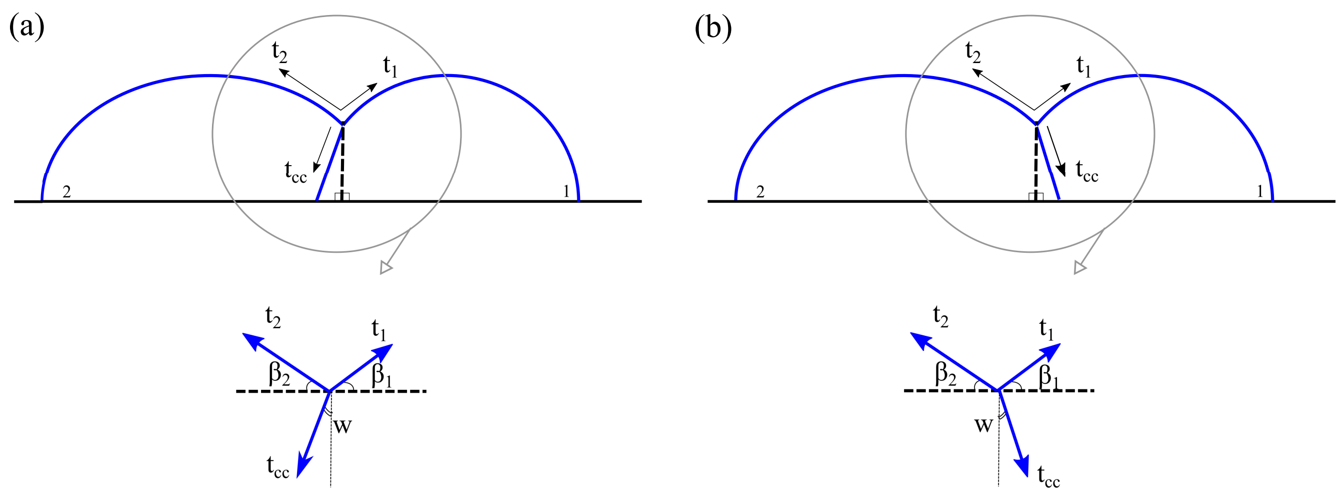

Figure 1. Side-view of the two cells. Two possibilities are considered including (a) negative w angle and (b) positive w angle.

1) FORCE BALANCE AT THE ENDPOINTS: protrusive forces are balanced by tension. Given f, t_1, t_2, t_0 and τ (*__plus a choice of__* v), obtain α_1, α_2

Force balance at the front endpoint of the leader cell:

(1.a) $$(1+f)\left(1-\frac{t_1}{t_0+\tau}\right)-v=t_1\cos\alpha_1$$

Force balance at the rear endpoint of the trailer cell:

(1.b) $$(1-f)\left(1-\frac{t_2}{t_0-\tau}\right)+v=t_2\cos\alpha_2$$

- [ ] *N.B. Should this force balance include the drag coefficient since it is included in the force balance at the bottom of the cell-cell region in Eq. 8 ?*

Then, we obtain:

(1.a) $$\alpha_1=\cos^{-1}\left[\frac{(1+f)}{t_1}\left(1-\frac{t_1}{t_0+\tau}\right)-\frac{v}{t_1}\right]$$

(1.b) $$\alpha_2=\cos^{-1}\left[\frac{(1-f)}{t_2}\left(1-\frac{t_2}{t_0-\tau}\right)+\frac{v}{t_2}\right]$$

Solvability conditions:

- $$-1\le\frac{(1+f)}{t_1}\left(1-\frac{t_1}{t_0+\tau}\right)-\frac{v}{t_1}\le 1\Rightarrow -t_1\le(1+f)\left(1-\frac{t_1}{t_0+\tau}\right)-v\le t_1$$

$$-t_1 \leq (1+f)\frac{t_0+\tau-t_1}{t_0+\tau} - \frac{v(t_0+\tau)}{t_0+\tau} \leq t_1 \Rightarrow -t_1(t_0+\tau) \leq (1+f)(t_0+\tau-t_1) - v(t_0+\tau) \leq t_1(t_0+\tau)$$

- Similarly, $-t_2(t_0-\tau) \leq (1-f)(t_0-\tau-t_2) - v(t_0-\tau) \leq t_2(t_0-\tau)$

Conditions:
- $t_0 \neq \tau$
- $\beta_1 < \alpha_1$ and $\beta_2 < \alpha_2$

2) FORCE BALANCE AT THE TOP OF CELL-CELL INTERACTION REGION given t_1, t_2 and t_{cc} (*plus a choice of* w) to obtain β_1, β_2

(2.a) $t_1 \cos\beta_1 - t_2 \cos\beta_2 + \dfrac{w}{|w|} t_{cc} \sin|w| = 0$ (x-direction)

(2.b) $t_1 \sin\beta_1 + t_2 \sin\beta_2 - t_{cc} \cos|w| = 0$ (y-direction)

Reduce to:

(2.a) $\beta_1 = \cos^{-1}\left(\dfrac{t_2}{t_1}\cos\beta_2 - \dfrac{w}{|w|}\dfrac{t_{cc}}{t_1}\sin|w|\right)$

(2.b) $t_1 \sin\left[\cos^{-1}\left(\dfrac{t_2}{t_1}\cos\beta_2 - \dfrac{w}{|w|}\dfrac{t_{cc}}{t_1}\sin|w|\right)\right] + t_2\sin\beta_2 - t_{cc}\cos|w| = 0$

Solve 2.b with fzero in Matlab for β_2. Then use equation 2.a to solve for β_1.

3) USE AREAS given $\alpha_1, \alpha_2, \beta_1$, and β_2 to find r_1 and r_2

From Fig. 2 the **shaded** area of the second cell (trailer) is

$$A_2 = \frac{\pi r_2^2}{2}\frac{(\alpha_2+\beta_2)}{\pi} - \frac{1}{2}r_2^2\sin\alpha_2\cos\alpha_2 - \frac{1}{2}r_2^2\cos^2\alpha_2\tan\beta_2 \equiv 1$$

which yields the following expressions for the radii:

(3.a) $r_1 = \left[\dfrac{(\alpha_1+\beta_1)}{2} - \dfrac{1}{2}\sin\alpha_1\cos\beta_1 - \dfrac{1}{2}\cos^2\alpha_1\tan\beta_1\right]^{-1/2}$

(3.b) $r_2 = \left[\dfrac{(\alpha_2+\beta_2)}{2} - \dfrac{1}{2}\sin\alpha_2\cos\beta_2 - \dfrac{1}{2}\cos^2\alpha_2\tan\beta_2\right]^{-1/2}$

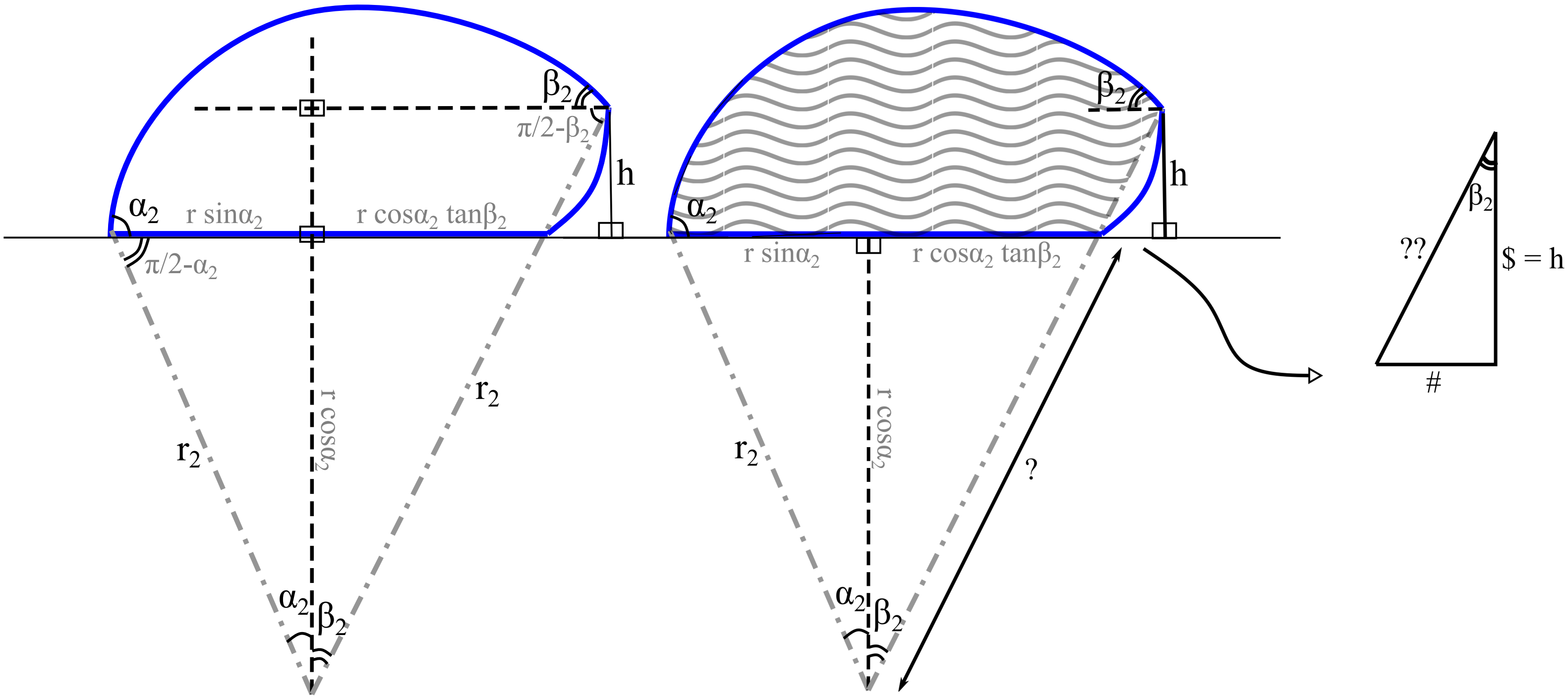

Figure 2. Zoom in of trailer cell to illustrate area computation for (3.b)

☑ *We can improve our area calculation slightly; including the small triangle on the right-side (not the arc section) in the area calculation produces*

$$A_2 = \frac{\pi r_2^2}{2}\frac{(\alpha_2+\beta_2)}{\pi} - \frac{1}{2}r_2^2 \sin\alpha_2 \cos\alpha_2 - \frac{1}{2}r_2^2 \cos^2\alpha_2 \tan\beta_2 + \frac{1}{2}r_2^2\Big(\cos\beta_2 - \cos\alpha_2 \tan\beta_2\Big)\Big(\sin\beta_2 - \cos\alpha_2 \tan^2\beta_2\Big) \equiv 1$$

The resulting radii are

(3.a)

$$r_1 = \left[\frac{(\alpha_1+\beta_1)}{2} - \frac{1}{2}\sin\alpha_1 \cos\beta_1 - \frac{1}{2}\cos^2\alpha_1 \tan\beta_1 + \frac{1}{2}\Big(\cos\beta_1 - \cos\alpha_1 \tan\beta_1\Big)\Big(\sin\beta_1 - \cos\alpha_1 \tan^2\beta_1\Big)\right]^{-1/2}$$

(3.b)

$$r_2 = \left[\frac{(\alpha_2+\beta_2)}{2} - \frac{1}{2}\sin\alpha_2 \cos\beta_2 - \frac{1}{2}\cos^2\alpha_2 \tan\beta_2 + \frac{1}{2}\Big(\cos\beta_2 - \cos\alpha_2 \tan\beta_2\Big)\Big(\sin\beta_2 - \cos\alpha_2 \tan^2\beta_2\Big)\right]^{-1/2}$$

4) FROM TRIGONOMETRY find the equation for the height of the cell-cell junction

(4.a) $h = h_1 = r_1\left(\cos\beta_1 - \cos\alpha_1\right)$

(4.b) $h = h_2 = r_2\left(\cos\beta_2 - \cos\alpha_2\right)$

or alternatively $r_1\left(\cos\beta_1 - \cos\alpha_1\right) = r_2\left(\cos\beta_2 - \cos\alpha_2\right)$.

One suggestion is to loop over steps 1-4 and adjust $w = w + \epsilon$ until $\delta h = |h_1 - h_2| \leq$ tolerance.

5) FROM LAPLACE'S LAW the intracellular pressure is:

$$p_1 = \frac{t_1}{r_1} \text{ and } p_2 = \frac{t_2}{r_2}$$

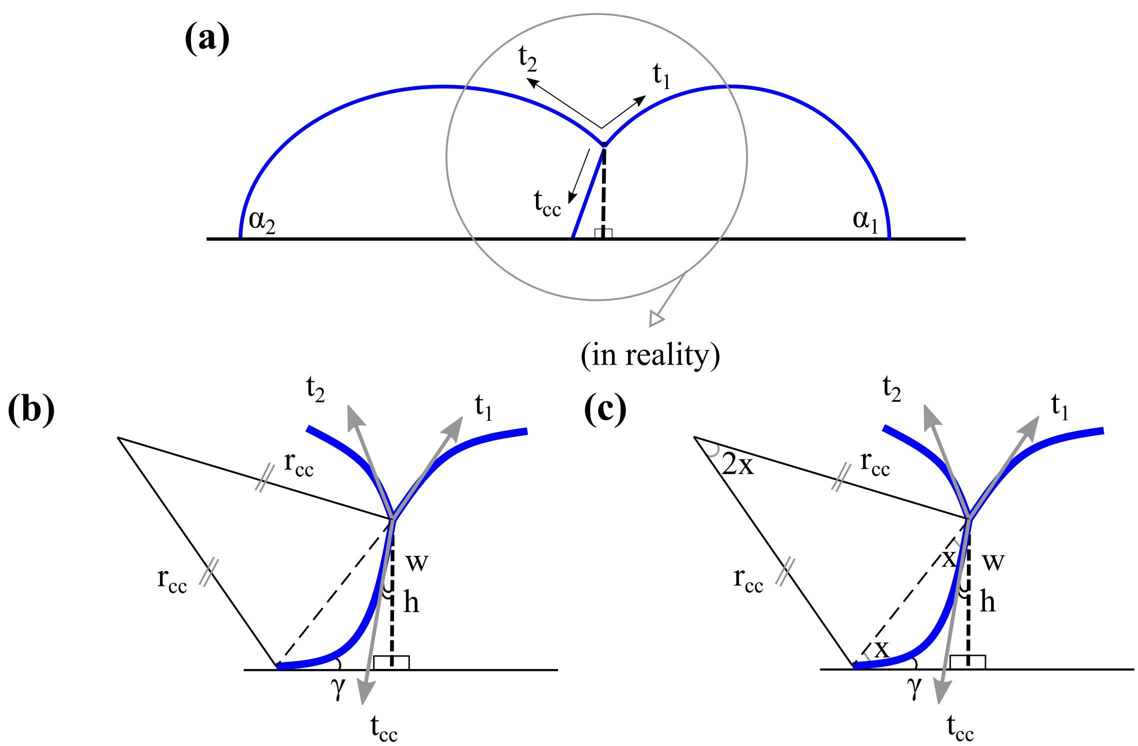

Figure 3. Zoom in of the cell-cell interface and the resulting angles in the wedge

6) FROM LAPLACE'S LAW find the radius of curvature for the cell-cell junction

$$p_2 - p_1 = \frac{t_{cc}}{r_{cc}} \rightarrow r_{cc} = \frac{t_{cc}}{t_2/r_2 - t_1/r_1}$$

7) USE TRIGONOMETRY AT CELL-CELL INTERFACE given h, w, r_{cc}, to find the angle γ at the ventral end of the cell-cell boundary

$$(1)\ \cos(|x| + |w|) = \frac{h}{s}$$

(2) $\sin(|x| + \gamma) = \dfrac{h}{s}$

(3) $s^2 = 2r_{cc}^2\,(1 - \cos(2|w|))$ (where s is the third side in the isosceles triangle with sides r_{cc})

Combining (1) and (3), to obtain:

$\dfrac{h^2}{\cos^2(|x| + |w|)} = 2r_{cc}^2\,\left(1 - \cos(2|x|)\right)$ fzero for $x \in [0, \pi/4]$.

Then: $\gamma = \dfrac{\pi}{2} - |w| - 2|x|$.

8) Lastly, γ is a function of v, or a constant. In any case, THE FORCE BALANCE AT THE VENTRAL END OF THE CELL-CELL REGION closes the system

$t_{cc}\cos(\gamma) = \xi v_{\text{end}} \Rightarrow v_{\text{end}} = \dfrac{t_{cc}}{\xi}\cos(\gamma)$

Now loop over steps 1-8 and adjust $v = v + \epsilon$ until $\delta v = |v - v_{\text{end}}| \leq$ tolerance.