Steady State Configurations of Cells Connected by Cadherin Sites

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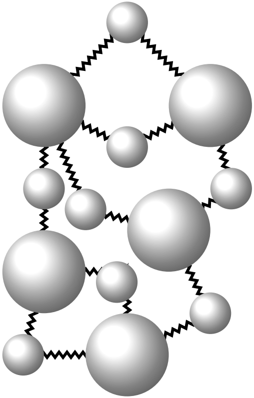
Setting

Goal

- Cells: $\mathbf{x}_i \in \mathbb{R}^2$ for $i = 1, \ldots, n$
- C-sites $\mathbf{c}_{i,j,k} \in \mathbb{R}^2$
  for $i, j = 1, \ldots, N$ and $k = 1, \ldots, n_{ij}$



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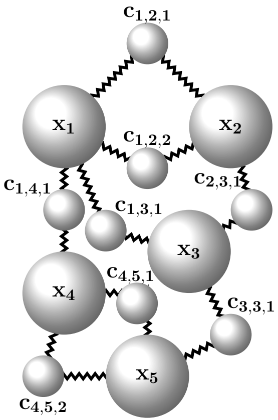
Parameters

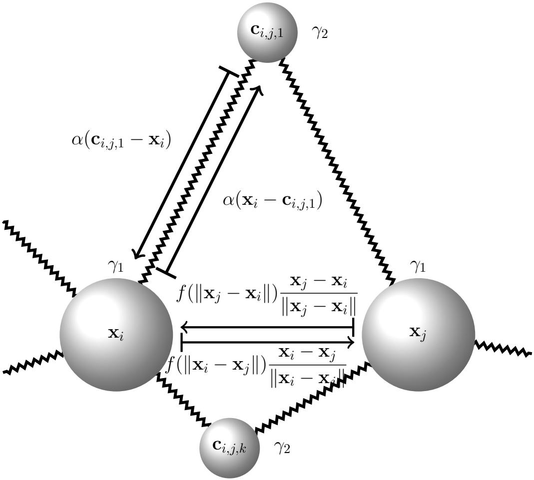
- Spring constant: α
- Cell drag coefficient: $\gamma_1 > 0$
- C-site drag coefficient: $\gamma_2 > 0$ $(\gamma_1 > \gamma_2)$



Formulation of the Model

Forces

- Body Force:
  $f : [0, \infty) \to \infty$
  decreasing, convex,
  supported over $[0, r]$,
  blows up at 0
- Hookean spring, zero rest length
- Drag, proportional to velocity



Formulation of the Model

- Newton's second Law of motion, applied to a cell:

$$
\begin{aligned}
m\ddot{\mathbf{x}}_i = & \sum_{\substack{j=1 \\ j\neq i}}^{n} f(\|\mathbf{x}_i - \mathbf{x}_j\|)\frac{\mathbf{x}_i - \mathbf{x}_j}{\|\mathbf{x}_i - \mathbf{x}_j\|} && \text{(body forces)} \\
& + \sum_{j=1}^{n}\sum_{k=1}^{n_{i,j}} \alpha(\mathbf{c}_{i,j,k} - \mathbf{x}_i) && \text{(c-site forces)} \\
& - \gamma_1 \dot{\mathbf{x}}_i && \text{(drag)}
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- Low Reynolds number environment implies $\ddot{\mathbf{x}}_i = 0$ for $i = 1, 2, \ldots, n$.
- Equations for c-sites are similarly derived.

Formulation of the Model

Equation of Motion of Cells and C-sites

$$\begin{cases} \gamma_1 \dot{\mathbf{x}}_i = & \sum_{\substack{j=1 \\ j\neq i}}^{n} f(\|\mathbf{x}_i - \mathbf{x}_j\|) \frac{\mathbf{x}_i - \mathbf{x}_j}{\|\mathbf{x}_i - \mathbf{x}_j\|} + \sum_{j=1}^{n} \sum_{k=1}^{n_{i,j}} \alpha(\mathbf{c}_{i,j,k} - \mathbf{x}_1) \\ \gamma_2 \dot{\mathbf{c}}_{i,j,k} = & \alpha(\mathbf{x}_i - \mathbf{c}_{i,j,k}) + \alpha(\mathbf{x}_j - \mathbf{c}_{i,j,k}) \end{cases}$$

$\mathbf{x}_i$ ranges over all the cells
$\mathbf{c}_{i,j,k}$ ranges over all the c-sites.

For $\boldsymbol{x} = (\mathbf{x}_1, \dots, \mathbf{x}_n, \dots, \mathbf{c}_{i,j,k}, \dots) \in \mathbb{R}^{2n+2m}$ we may easily rewrite the system to be of the form

$$\dot{\boldsymbol{x}} = \boldsymbol{f}(\boldsymbol{x}).$$

Center of Drag

Definition

In a cell system with $\boldsymbol{x} = (\mathbf{x}_1, \dots, \mathbf{x}_n, \dots, \mathbf{c}_{i,j,k}, \dots) \in \mathbb{R}^{2n+2m}$ the *center of drag of the cell system* is defined to be the point

$$\mathbf{x}_{\text{cod}} = \frac{\displaystyle\sum_{i=1}^{n} \gamma_i \mathbf{x}_i + \sum_{i<j} \sum_{k=1}^{n_{i,j}} \gamma_{i,j,k} \mathbf{c}_{i,j,k}}{\displaystyle\sum_{i=1}^{n} \gamma_i + \sum_{i<j} \sum_{k=1}^{n_{i,j}} \gamma_{i,j,k}}.$$

Proposition

In our set up, the center of drag is conserved throughout the entire evolution of that system.

Existence and Uniqueness

We classify certain parameter spaces:

Definition (Type 1)

- Function f as stated
- Cells share common drag coefficient γ_1
- C-sites share common drag coefficient γ_2
- One common spring constant α

Definition (Type 2)

- Function f as stated
- Cells share common drag coefficient γ_1
- C-sites drag coefficients may vary between sites
- Spring constants also may vary

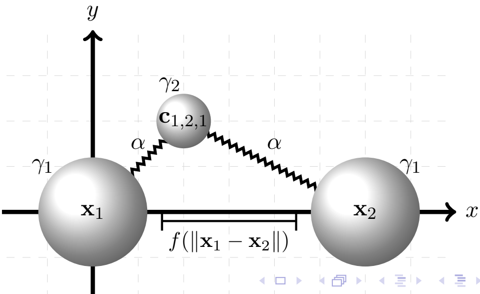
Theorem (Global Existence and Uniqueness)

For problems of type 2 there exist a unique solution on $[0, \infty)$.

Hookean Cell Systems of Two Cells and One c-Site

Let $\hat{\mathfrak{H}}$ be the Hookean Cell Systems of Two Cells and One c-Site given by

$$\begin{cases} \gamma_1 \dot{\mathbf{x}}_1 = & f(\|\mathbf{x}_1 - \mathbf{x}_2\|)\frac{\mathbf{x}_1 - \mathbf{x}_2}{\|\mathbf{x}_1 - \mathbf{x}_2\|} + \alpha(\mathbf{c} - \mathbf{x}_1) \\ \gamma_1 \dot{\mathbf{x}}_2 = & f(\|\mathbf{x}_1 - \mathbf{x}_2\|)\frac{\mathbf{x}_2 - \mathbf{x}_1}{\|\mathbf{x}_1 - \mathbf{x}_2\|} + \alpha(\mathbf{c} - \mathbf{x}_2) \\ \gamma_2 \dot{\mathbf{c}} = & \alpha(\mathbf{x}_1 - \mathbf{c}) + \alpha(\mathbf{x}_2 - \mathbf{c}) \\ \mathbf{x}_1(0) = (0,0), & \mathbf{x}_2(0) = (l,0), \text{ and } \mathbf{c}(0) = (x_c(0), y_c(0)). \end{cases}$$



Two Regimes

It is useful to consider the problem in two cases:

Regime 1. $\|\mathbf{x}_2 - \mathbf{x}_1\| \geq r$ (linear)

Regime 2. $\|\mathbf{x}_2 - \mathbf{x}_1\| < r$ (Nonlinear)

Regime 1: beyond the Support of f

In this regime the system may be written without the body force terms, seen here

$$\begin{cases} \gamma_1 \dot{\mathbf{x}}_1 = & \alpha(\mathbf{c} - \mathbf{x}_1) \\ \gamma_1 \dot{\mathbf{x}}_2 = & \alpha(\mathbf{c} - \mathbf{x}_2) \\ \gamma_2 \dot{\mathbf{c}} = & \alpha(\mathbf{x}_1 - \mathbf{c}) + \alpha(\mathbf{x}_2 - \mathbf{c}) \\ \mathbf{x}_1 = (0,0), \mathbf{x}_2 = (l,0), \mathbf{c} = (x_c(0), y_c(0)) \end{cases}$$

where $l > r$. We solved this by nondimensionalizing the system and then using elementary differential equations techniques.

The Solution

$$x_1(t) = \frac{x_c(0)\gamma_2 + l\gamma_1}{2\gamma_1+\gamma_2} - \frac{l}{2}e^{-\alpha t/\gamma_1} - \frac{2x_c(0)\gamma_2 - l\gamma_2}{2(2\gamma_1+\gamma_2)}e^{-\alpha(\gamma_1^{-1}+2\gamma_2^{-1})t}$$

$$y_1(t) = \frac{y_c(0)\gamma_2}{2\gamma_1+\gamma_2} - \frac{y_c(0)\gamma_2}{2\gamma_1+\gamma_2}e^{-\alpha(\gamma_1^{-1}+2\gamma_2^{-1})t}$$

$$x_2(t) = \frac{x_c(0)\gamma_2 + l\gamma_1}{2\gamma_1+\gamma_2} + \frac{l}{2}e^{-\alpha t/\gamma_1} - \frac{2x_c(0)\gamma_2 - l\gamma_2}{2(2\gamma_1+\gamma_2)}e^{-\alpha(\gamma_1^{-1}+2\gamma_2^{-1})t}$$

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This then provides the exact values of $\boldsymbol{x}$, at least until $\boldsymbol{x}$ leaves the set $\theta_{2,r} \times \mathbb{R}^2$.

Analysis of the Solution

Observation 1

First of all note that y_1 and y_2 are identical: no rotation occurs between the two cells. (in regime 1)

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The path that $\mathbf{c}$ travels is a line.

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Observation 2

The path that $\mathbf{c}$ travels is a line.

Observation 3

$$\|\mathbf{x}_1(t) - \mathbf{x}_2(t)\| = le^{-\alpha t/\gamma_1}$$

We may determine precisely when and where the system will exit regime 1.

Regime 2: Within the Support of f

We analyze this nonlinear system in a few steps.

1 Find equilibria of the system.

2 Determine stability.

2 Use this information (and work in regime 1) to guess at solutions. (If solutions are valid they are unique)

The Equilibria of $\dot{\boldsymbol{x}} = \boldsymbol{f}(\boldsymbol{x})$

To solve for the equilibria (if any) of the nonlinear system set the derivative terms equal to $\mathbf{0}$. So, that

$$\mathbf{0} = \boldsymbol{f}(\boldsymbol{x})$$

or

$$\begin{aligned}
\mathbf{0} =& f(\|\mathbf{x}_1 - \mathbf{x}_2\|)\frac{\mathbf{x}_1 - \mathbf{x}_2}{\|\mathbf{x}_1 - \mathbf{x}_2\|} + \alpha(\mathbf{c} - \mathbf{x}_1)\\
\mathbf{0} =& f(\|\mathbf{x}_1 - \mathbf{x}_2\|)\frac{\mathbf{x}_2 - \mathbf{x}_1}{\|\mathbf{x}_1 - \boldsymbol{x}_2\|} + \alpha(\mathbf{c} - \mathbf{x}_2)\\
\mathbf{0} =& \alpha(\mathbf{x}_1 - \mathbf{c}) + \alpha(\mathbf{x}_2 - \mathbf{c}).
\end{aligned}$$

The last equation will only be satisfied if

$$\mathbf{c} = \frac{\mathbf{x}_1 + \mathbf{x}_2}{2}.$$

The Equilibria of $\dot{x} = f(x)$

Substituting this for $\mathbf{c}$ into the first and second equations reduces the system to

$$\mathbf{0} = f(\|\mathbf{x}_1 - \mathbf{x}_2\|)\frac{\mathbf{x}_1 - \mathbf{x}_2}{\|\mathbf{x}_1 - \mathbf{x}_2\|} + \alpha\left(\frac{\mathbf{x}_2 - \mathbf{x}_1}{2}\right)$$

$$\mathbf{0} = f(\|\mathbf{x}_1 - \mathbf{x}_2\|)\frac{\mathbf{x}_2 - \mathbf{x}_1}{\|\mathbf{x}_1 - \mathbf{x}_2\|} + \alpha\left(\frac{\mathbf{x}_1 - \mathbf{x}_2}{2}\right)$$

or more simply

$$\mathbf{0} = \left(\frac{f(\|\mathbf{x}_1 - \mathbf{x}_2\|)}{\|\mathbf{x}_1 - \mathbf{x}_2\|} - \frac{\alpha}{2}\right)(\mathbf{x}_1 - \mathbf{x}_2)$$

$$\mathbf{0} = \left(\frac{f(\|\mathbf{x}_1 - \mathbf{x}_2\|)}{\|\mathbf{x}_1 - \mathbf{x}_2\|} - \frac{\alpha}{2}\right)(\mathbf{x}_2 - \mathbf{x}_1).$$

The Equilibria of $\dot{\boldsymbol{x}} = \boldsymbol{f}(\boldsymbol{x})$

And so,

$$\frac{f(\|\mathbf{x}_1 - \mathbf{x}_2\|)}{\|\mathbf{x}_1 - \mathbf{x}_2\|} - \frac{\alpha}{2} = 0,$$

or

$$2f(\Delta x) = \alpha \Delta x, \qquad (\Delta x = \|\mathbf{x}_1 - \mathbf{x}_2\|)$$

Define r_0 be the unique fixed point of $\frac{2}{\alpha} f$.

Necessary and sufficient conditions for the critical points

$\boldsymbol{x} \in \mathbb{R}^6$ is a cricitcal point if and only if

$$(1) \qquad \mathbf{c} = \frac{\mathbf{x}_1 + \mathbf{x}_2}{2} \qquad \text{and}$$

$$(2) \qquad \|\mathbf{x}_1 - \mathbf{x}_2\| = r_0.$$

The Equilibria of $\dot{\boldsymbol{x}} = \boldsymbol{f}(\boldsymbol{x})$

Let $c(\boldsymbol{f})$ denote the set of equilibria of $\dot{\boldsymbol{x}} = \boldsymbol{f}(\boldsymbol{x})$. It can be shown

$$\bigcup_{\theta \in \mathbb{R}} L_\theta \left(\boldsymbol{x}^0 + W\right) = c(\boldsymbol{f}),$$

where

$$W = \text{span}\left\{ \begin{pmatrix} 1 \\ 0 \\ 1 \\ 0 \\ 1 \\ 0 \end{pmatrix}, \begin{pmatrix} 0 \\ 1 \\ 0 \\ 1 \\ 0 \\ 1 \end{pmatrix} \right\}, \quad \text{and} \quad \boldsymbol{x}^0 = \begin{pmatrix} 0 \\ 0 \\ r_0 \\ 0 \\ \frac{r_0}{2} \\ 0 \end{pmatrix}$$

The Equilibria of $\dot{\boldsymbol{x}} = \boldsymbol{f}(\boldsymbol{x})$

Theorem

$c(\boldsymbol{f})$ is a smooth submanifold of $\mathbb{R}^{2n+2m}$

The above formulation of $c(\boldsymbol{f})$ recommends that it may be the image of a functions and in fact it is $G : \mathbb{R}^3 \to c(\boldsymbol{f}) \subset \mathbb{R}^6$ by

$$G(x_a, y_a, \theta) = \begin{pmatrix} \frac{r_0}{2}\cos\theta + \frac{r_0}{2} + x_a \\ \frac{r_0}{2}\sin\theta + y_a \\ \frac{r_0}{2}\cos(\theta+\pi) + \frac{r_0}{2} + x_a \\ \frac{r_0}{2}\sin(\theta+\pi) + y_a \\ x_a + \frac{r_0}{2} \\ y_a \end{pmatrix},$$

Notice G is smooth and its first partials exists.

The Equilibria of $\dot{x} = f(x)$

These partials taken at some point (x_a, y_a, θ) provide a basis for the tangent space at $G(x_a, y_a, \theta)$. This basis is developed below:

$$G_{x_a} = \begin{pmatrix} 1 \\ 0 \\ 1 \\ 0 \\ 1 \\ 0 \end{pmatrix}, \; G_{y_a} = \begin{pmatrix} 0 \\ 1 \\ 0 \\ 1 \\ 0 \\ 1 \end{pmatrix}, \text{ and } G_\theta = \begin{pmatrix} -\frac{r_0}{2}\sin\theta \\ \frac{r_0}{2}\cos\theta \\ -\frac{r_0}{2}\sin(\theta+\pi) \\ \frac{r_0}{2}\cos(\theta+\pi) \\ 0 \\ 0 \end{pmatrix}.$$

The Equilibria of $\dot{\boldsymbol{x}} = \boldsymbol{f}(\boldsymbol{x})$

Simplifying G_θ the basis of the tangent space of $c(\boldsymbol{f})$ at some point (x_a, y_a, θ) is

$$\left\{ \begin{pmatrix} 1 \\ 0 \\ 1 \\ 0 \\ 1 \\ 0 \end{pmatrix}, \begin{pmatrix} 0 \\ 1 \\ 0 \\ 1 \\ 0 \\ 1 \end{pmatrix}, \begin{pmatrix} \tan\theta \\ -1 \\ -\tan\theta \\ 1 \\ 0 \\ 0 \end{pmatrix} \right\}.$$

The Stability of the equilibria

In order to study the stability of these equilibria it will be useful to simplify $\boldsymbol{f}$ by defining a function $g : \mathbb{R}^4 \to \mathbb{R}$ as

$$g(x_1, y_1, x_2, y_2) = g(\mathbf{x}_1, \mathbf{x}_2) = \frac{f(\|\mathbf{x}_1 - \mathbf{x}_2\|)}{\gamma_1 \|\mathbf{x}_1 - \mathbf{x}_2\|}.$$

This way,

$$\boldsymbol{f}(\boldsymbol{x}) = \begin{pmatrix} \left(g(\mathbf{x}_1, \mathbf{x}_2) - \frac{\alpha}{\gamma_1}\right)\mathbf{x}_1 & -g(\mathbf{x}_1, \mathbf{x}_2)\mathbf{x}_2 & +\frac{\alpha}{\gamma_1}\mathbf{c} \\ -g(\mathbf{x}_1, \mathbf{x}_2)\mathbf{x}_1 & +\left(g(\mathbf{x}_1, \mathbf{x}_2) - \frac{\alpha}{\gamma_1}\right)\mathbf{x}_2 & +\frac{\alpha}{\gamma_1}\mathbf{c} \\ \frac{\alpha}{\gamma_2}\mathbf{x}_1 & +\frac{\alpha}{\gamma_2}\mathbf{x}_2 & -\frac{2\alpha}{\gamma_2}\mathbf{c} \end{pmatrix}.$$

The Stability of the equilibria

So, then $\mathbf{D}\boldsymbol{f}(\tilde{\boldsymbol{x}})$ may be expressed as

$$\frac{f'(r_0)-\frac{\alpha}{2}}{\gamma_1 r_0^2}\begin{pmatrix} (\Delta x)^2 & \Delta x\Delta y & -(\Delta x)^2 & -\Delta x\Delta y & 0 & 0 \\ \Delta x\Delta y & (\Delta y)^2 & -\Delta x\Delta y & -(\Delta y)^2 & 0 & 0 \\ (\Delta x)^2 & \Delta x\Delta y & -(\Delta x)^2 & -\Delta x\Delta y & 0 & 0 \\ \Delta x\Delta y & (\Delta y)^2 & -\Delta x\Delta y & -(\Delta y)^2 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \end{pmatrix}$$

$$+\frac{\alpha}{2\gamma_1}\begin{pmatrix} -1 & 0 & -1 & 0 & 2 & 0 \\ 0 & -1 & 0 & -1 & 0 & 2 \\ -1 & 0 & -1 & 0 & 2 & 0 \\ 0 & -1 & 0 & -1 & 0 & 2 \\ 2\frac{\gamma_1}{\gamma_2} & 0 & 2\frac{\gamma_1}{\gamma_2} & 0 & -4\frac{\gamma_1}{\gamma_2} & 0 \\ 0 & 2\frac{\gamma_1}{\gamma_2} & 0 & 2\frac{\gamma_1}{\gamma_2} & 0 & -4\frac{\gamma_1}{\gamma_2} \end{pmatrix}$$

where $\Delta x = \tilde{x}_1 - \tilde{x}_2$ and $\Delta y = \tilde{y}_1 - \tilde{y}_2$.

The Stability of the equilibria

The eigenvalues of $\mathbf{D}\boldsymbol{f}(\tilde{\boldsymbol{x}})$ are
$0, 0, 0, -\alpha\left(\frac{1}{\gamma_1}+\frac{2}{\gamma_2}\right), -\alpha\left(\frac{1}{\gamma_1}+\frac{2}{\gamma_2}\right), \frac{1}{\gamma_1}\left(f'(r_0)-\frac{\alpha}{2}\right)$
The eigenvectors of the zero eigenvalues are:

$$\begin{pmatrix} 0 \\ 1 \\ 0 \\ 1 \\ 0 \\ 1 \end{pmatrix}, \begin{pmatrix} 1 \\ 0 \\ 1 \\ 0 \\ 1 \\ 0 \end{pmatrix}, \text{ and } \begin{pmatrix} \frac{y_1-y_2}{x_1-x_2} \\ -1 \\ -\frac{y_1-y_2}{x_1-x_2} \\ 1 \\ 0 \\ 0 \end{pmatrix}.$$

It should be noted that $\dfrac{y_1-y_2}{x_1-x_2}=\tan\theta$. (this is because θ from the parameterization of $c(\boldsymbol{f})$ was defined to be the angle from the positive x-axis the solution was rotated counterclockwise)

The Stability of the equilibria

What does this mean?

- $c(\boldsymbol{f}) = U_c$ (The center manifold and the set of equilibria of $\dot{\boldsymbol{x}} = \boldsymbol{f}(\boldsymbol{x})$ are the same.)

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- $c(\boldsymbol{f}) = U_c$ (The center manifold and the set of equilibria of $\dot{\boldsymbol{x}} = \boldsymbol{f}(\boldsymbol{x})$ are the same.)
- There is no unstable manifold. (Since all of the nonzero eigenvalues of $\mathbf{D}\boldsymbol{f}(\tilde{\boldsymbol{x}})$ are negative.)
- All the equilibria are stable.

The solution to our system

$$\begin{cases} \gamma_1 \dot{\mathbf{x}}_1 = & f(\|\mathbf{x}_1 - \mathbf{x}_2\|)\frac{\mathbf{x}_1 - \mathbf{x}_2}{\|\mathbf{x}_1 - \mathbf{x}_2\|} + \alpha(\mathbf{c} - \mathbf{x}_1) \\ \gamma_1 \dot{\mathbf{x}}_2 = & f(\|\mathbf{x}_1 - \mathbf{x}_2\|)\frac{\mathbf{x}_2 - \mathbf{x}_1}{\|\mathbf{x}_1 - \mathbf{x}_2\|} + \alpha(\mathbf{c} - \mathbf{x}_2) \\ \gamma_2 \dot{\mathbf{c}} = & \alpha(\mathbf{x}_1 - \mathbf{c}) + \alpha(\mathbf{x}_2 - \mathbf{c}) \\ \mathbf{x}_1(0) = (0,0), & \mathbf{x}_2(0) = (l,0), \text{ and } \quad \mathbf{c}(0) = (x_c(0), y_c(0)). \end{cases}$$

Let $g(x_1, x_2, y_1, y_2) = f(\|\mathbf{x}_1 - \mathbf{x}_2\|)/\|\mathbf{x}_1 - \mathbf{x}_2\|$, and get

$$\begin{cases} \gamma_1 \dot{x}_1 = & g(x_1, x_2, y_1, y_2)(x_1 - x_2) + \alpha(x_c - x_1) \\ \gamma_1 \dot{y}_1 = & g(x_1, x_2, y_1, y_2)(y_1 - y_2) + \alpha(y_c - y_1) \\ \gamma_1 \dot{x}_2 = & g(x_1, x_2, y_1, y_2)(x_2 - x_1) + \alpha(x_c - x_2) \\ \gamma_1 \dot{y}_2 = & g(x_1, x_2, y_1, y_2)(y_2 - y_1) + \alpha(y_c - y_1) \\ \gamma_2 \dot{x}_c = & \alpha(x_1 - x_c) + \alpha(x_2 - x_c) \\ \gamma_2 \dot{y}_c = & \alpha(y_1 - y_c) + \alpha(y_2 - y_c). \\ x_1(0) = 0, \ y_1(0) = 0, \ x_2(0) = l, \ y_2(0) = 0, \\ x_c(0) = c_x, \text{ and } y_c(0) = c_y. \end{cases}$$

The solution to our system

We make a shrewd guess: $y_1(t) = y_2(t) =: y(t)$ (This is possible since $y_1(0) = y_2(0) = 0$)
Isolate the y-components and solve

$$\begin{cases} \gamma_1 \dot{y}_1 = & g(x_1, x_2, y_1, y_2)(y_1 - y_2) + \alpha(y_c - y_1) \\ \gamma_1 \dot{y}_2 = & g(x_1, x_2, y_1, y_2)(y_2 - y_1) + \alpha(y_c - y_1) \\ \gamma_2 \dot{y}_c = & \alpha(y_1 - y_c) + \alpha(y_2 - y_c). \\ y_1(0) = 0,\ y_2(0) = 0,\ y_c(0) = c_y. \end{cases}$$

becomes

$$\begin{cases} \gamma_1 \dot{y} = & \alpha(y_c - y) \\ \gamma_2 \dot{y}_c = & 2\alpha(y - y_c) \\ y(0) = 0,\ y_c(0) = c_y. \end{cases}$$

This wins us $y_1(t)$, $y_2(t)$, and $y_c(t)$.

The solution to our system

We then use the conservation of the center of drag to relate $x_1(t)$, $x_2(t)$, and $x_c(t)$, in

$$\frac{\gamma_1 x_1(t) + \gamma_1 x_2(t) + \gamma_2 x_c(t)}{2\gamma_1 + \gamma_2} = \frac{x_c(0)\gamma_2 + l\gamma_1}{2\gamma_1 + \gamma_2}. \tag{1}$$

Plugging this into the $x_c(t)$ equation of the system (which is linear)

$$\gamma_2 \dot{x}_c = \alpha(x_1 - x_c) + \alpha(x_2 - x_c),$$

allows us to find $x_c(t)$ explicitly.

This gives a relation between $x_1(t)$ and $x_2(t)$ which can be used in conjunction with

$$\gamma_1 \dot{x}_1 = g(x_1, x_2, y_1, y_2)(x_1 - x_2) + \alpha(x_c - x_1)$$

to solve $x_1(t)$.

The solution to our system

- $x_1(t)$ satisfies the differential equation:

$$\gamma_1 \dot{x}_1 = -f\left(2x_1 - l - \frac{2\gamma_2 x_c(0) - l\gamma_2}{2\gamma_1+\gamma_2}\left(1 - e^{-\alpha(\gamma_1^{-1}+2\gamma_2^{-1})t}\right)\right) + \alpha\left(\frac{x_c(0)\gamma_2 + l\gamma_1}{2\gamma_1+\gamma_2} + \frac{2x_c(0)\gamma_1 - l\gamma_1}{2\gamma_1+\gamma_2}e^{-\alpha(\gamma_1^{-1}+2\gamma_2^{-1})t} - x_1\right)$$

  with $x_1(0) = 0$.
- $x_2 = l - x_1 + \frac{\gamma_2}{\gamma_1}(x_c(0) - x_c(t))$.
- $y_1(t) = \frac{y_c(0)\gamma_2}{2\gamma_1+\gamma_2} - \frac{y_c(0)\gamma_2}{2\gamma_1+\gamma_2}e^{-\alpha(\gamma_1^{-1}+2\gamma_2^{-1})t}$
- $y_2(t) = \frac{y_c(0)\gamma_2}{2\gamma_1+\gamma_2} - \frac{y_c(0)\gamma_2}{2\gamma_1+\gamma_2}e^{-\alpha(\gamma_1^{-1}+2\gamma_2^{-1})t}$
- $x_c(t) = \frac{x_c(0)\gamma_2 + l\gamma_1}{2\gamma_1+\gamma_2} + \frac{2x_c(0)\gamma_1 - l\gamma_1}{2\gamma_1+\gamma_2}e^{-\alpha(\gamma_1^{-1}+2\gamma_2^{-1})t}$
- $y_c(t) = \frac{y_c(0)\gamma_2}{2\gamma_1+\gamma_2} + \frac{2y_c(0)\gamma_1}{2\gamma_1+\gamma_2}e^{-\alpha(\gamma_1^{-1}+2\gamma_2^{-1})t}$

C-site Reduction Theorem for Two Cells

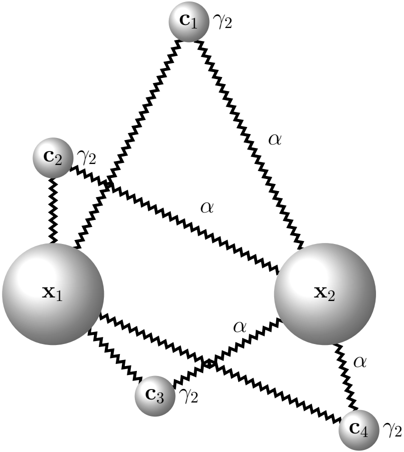
The theorem states that the several c-site problem:

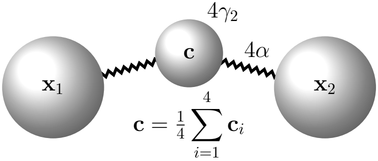
$$\begin{cases} \gamma_1 \dot{\mathbf{x}}_1 = & f(\|\mathbf{x}_1 - \mathbf{x}_2\|) \frac{\mathbf{x}_1 - \mathbf{x}_2}{\|\mathbf{x}_1 - \mathbf{x}_2\|} + \sum_{i=1}^{m} \alpha(\mathbf{c}_i - \mathbf{x}_1) \\ \gamma_1 \dot{\mathbf{x}}_2 = & f(\|\mathbf{x}_1 - \mathbf{x}_2\|) \frac{\mathbf{x}_2 - \mathbf{x}_1}{\|\mathbf{x}_1 - \mathbf{x}_2\|} + \sum_{i=1}^{m} \alpha(\mathbf{c}_i - \mathbf{x}_2) \\ \gamma_2 \dot{\mathbf{c}}_1 = & \alpha(\mathbf{x}_1 - \mathbf{c}_1) + \alpha(\mathbf{x}_2 - \mathbf{c}_1) \\ \vdots & \\ \gamma_2 \dot{\mathbf{c}}_m = & \alpha(\mathbf{x}_1 - \mathbf{c}_m) + \alpha(\mathbf{x}_2 - \mathbf{c}_m) \\ \boldsymbol{x}(0) = ((0,0),(l,0),\mathbf{c}_1(0),\mathbf{c}_2(0),\ldots,\mathbf{c}_m(0))^T & \end{cases}$$

prescribes the same <u>cell</u> movement as the reduced cell system:

$$\begin{cases} \gamma_1 \dot{\mathbf{x}}_1 = & f(\|\mathbf{x}_1 - \mathbf{x}_2\|) \frac{\mathbf{x}_1 - \mathbf{x}_2}{\|\mathbf{x}_1 - \mathbf{x}_2\|} + \sum_{i=1}^{m} \alpha(\mathbf{c}_i - \mathbf{x}_1) \\ \gamma_1 \dot{\mathbf{x}}_2 = & f(\|\mathbf{x}_1 - \mathbf{x}_2\|) \frac{\mathbf{x}_2 - \mathbf{x}_1}{\|\mathbf{x}_1 - \mathbf{x}_2\|} + \sum_{i=1}^{m} \alpha(\mathbf{c}_i - \mathbf{x}_2) \\ m\gamma_2 \dot{\mathbf{c}} = & m\alpha(\mathbf{x}_1 - \mathbf{c}) + m\alpha(\mathbf{x}_2 - \mathbf{c}) \\ \boldsymbol{x}(0) = \left((0,0),(l,0),\frac{1}{m}\sum_{k=1}^{m} \mathbf{c}_k(0)\right)^T & \end{cases}$$

C-site Reduction Theorem for Two Cells





C-site Reduction Theorem for Two Cells

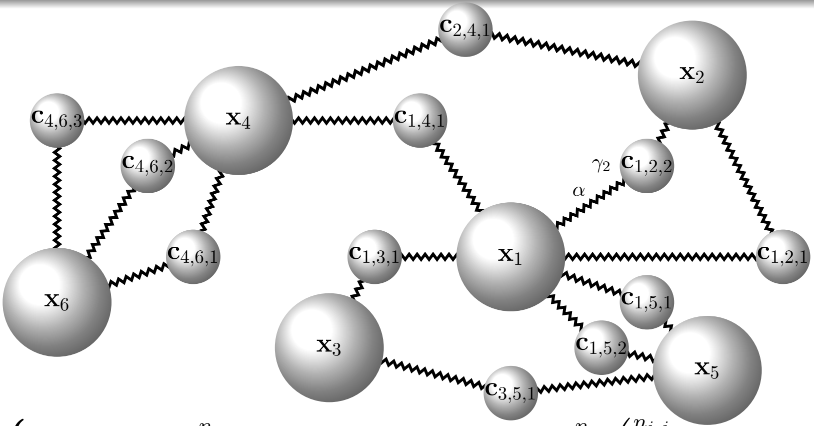
Sketch of proof:

- Let $\boldsymbol{x}(t) = (\mathbf{x}_1(t), \mathbf{x}_2(t), \mathbf{c}_1, \ldots, \mathbf{c}_m)$ be the unique solution to the several c-site problem.
- Verify that

$$\tilde{\boldsymbol{x}}(t) = \left(\mathbf{x}_1(t), \mathbf{x}_2(t), \frac{1}{m}\sum_{k=1}^{m} \mathbf{c}_k(t)\right)$$

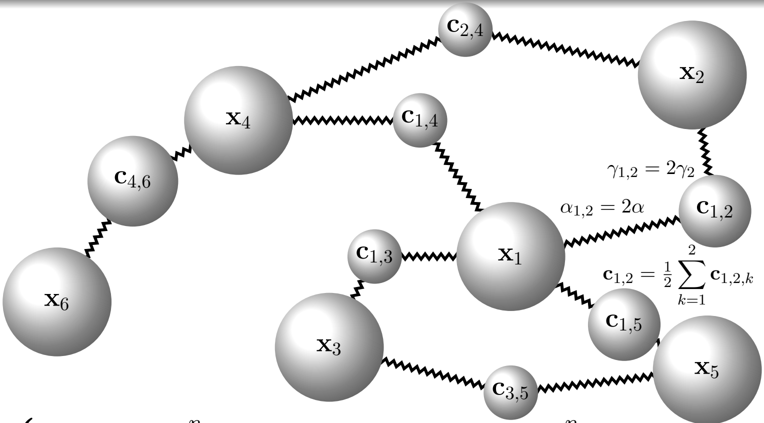
  is the unique solution to the reduced c-site problem, with the appropriate parameters ($m\alpha$ for spring constants, $m\gamma$ for drag coefficient)

General C-site Reduction Theorem



$$\begin{cases} \gamma_1 \dot{\boldsymbol{x}}_j = & \displaystyle\sum_{i=1}^{n} f(\|\boldsymbol{x}_j - \boldsymbol{x}_i\|) \frac{\boldsymbol{x}_j - \boldsymbol{x}_i}{\|\boldsymbol{x}_j - \boldsymbol{x}_i\|} + \sum_{i=1}^{n} \left(\sum_{k=1}^{n_{i,j}} \alpha(\boldsymbol{c}_{i,j,k} - \boldsymbol{x}_j) \right) \\ \gamma_2 \dot{\boldsymbol{c}}_{i,j,k} = & \alpha(\boldsymbol{x}_i - \boldsymbol{c}_{i,j,k}) + \alpha(\boldsymbol{x}_j - \boldsymbol{c}_{i,j,k}). \end{cases}$$

General C-site Reduction Theorem



$$\begin{cases} \gamma_1 \dot{\boldsymbol{x}}_j = \displaystyle\sum_{i=1}^{n} f(\|\boldsymbol{x}_j - \boldsymbol{x}_i\|) \frac{\boldsymbol{x}_j - \boldsymbol{x}_i}{\|\boldsymbol{x}_j - \boldsymbol{x}_i\|} + \sum_{i=1}^{n} \alpha n_{i,j} \left(\boldsymbol{c}_{i,j} - \boldsymbol{x}_j\right) \\ \gamma_2 n_{i,j} \dot{\boldsymbol{c}}_{i,j} = \alpha n_{i,j} \left(\boldsymbol{x}_i - \boldsymbol{c}_{i,j}\right) + \alpha n_{i,j} \left(\boldsymbol{x}_j - \boldsymbol{c}_{i,j}\right) \end{cases}$$

Conclusion and Future Work

Some questions of interest to us are:

1. What are the equilibria of a Hookean cell system of n cells?
2. What is the behavior of the system at that equilibria?
3. What is the next step in modifying the model to make it a closer approximation of the motion of a slug?
4. How can stochastics be introduced to such a frame work?