# Steady State Configurations of Cells Connected by Cadherin Sites

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# Overview

# Dictyostelium discoideum

In 1933 Dr. Kenneth B. Raper discovered *Dictyostelium discoideum* (Dd).

Figure: *Raper, Kenneth B.*, Lewellyn, Stephen - http://photoarchive.lib.uchicago.edu/

Dd is a eukaryotic, soil-living amoeba that transitions from a collection of single cellular organisms into a multicellular reproductive structure.

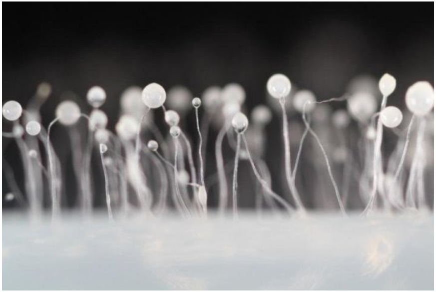


Figure: Strassmann/Queller lab - https://www.sciencedaily.com/ releases/2016/04/160421100822.htm

# Dictyostelium discoideum

Motility in Dd involves periodic extension and retraction of pseudopodia with coordinated adhesion to propel cellular movement in random directions.

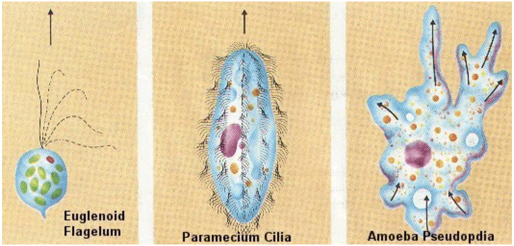
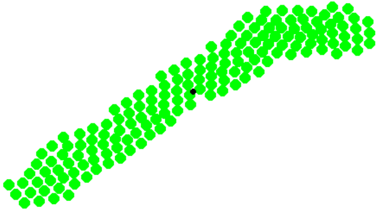



Figure: *tigermovement*, ©Cmassengale - http://www.biologyjunction.com/protozoan_notes_b1.htm

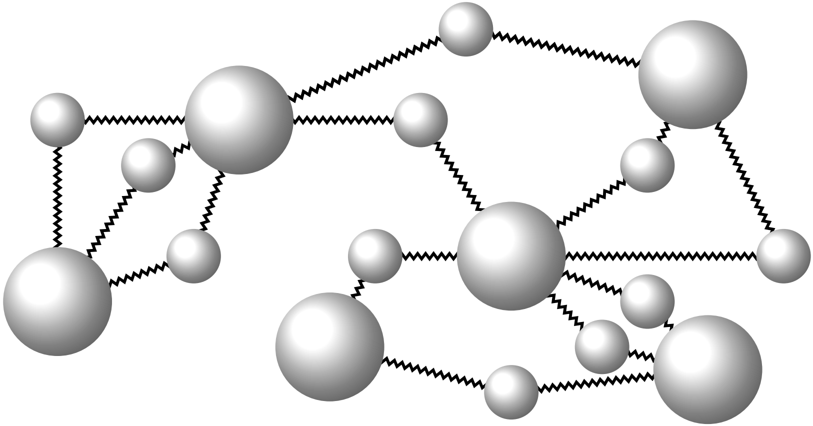
# Dictyostelium discoideum

For the past 8 years, Dr. John Dallon (BYU) has been researching Dd, and has employed students in developing computer simulations in order to better understand the movement of a population of cells like Dd.



These simulations have produced interesting results. We would like to better understand the elongation of the slug *in silico*.

## Cells and C-sites and How they Interact



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3. The spring constant for the springs that model the pseudopodia are all the same.
4. The cells possess an strong inhibition to occupy the same space.
5. There is no boundary to the plane on which the cell centers reside.
6. The c-sites are constantly attached to the cells.

## Notation

- Let $\mathbf{x}_i = \mathbf{x}_i(t)$, for real $t \geq 0$ and for $i = 1, 2, \ldots, n$, be points in $\mathbb{R}^2$ that denote the locations of the centers of $n$ cells at time $t$. The coordinates for the cell locations will be designated by $\mathbf{x}_i = (x_i, y_i)$.

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- Let $\mathbf{c}_{i,j,k} = \mathbf{c}_{i,j,k}(t)$ be the point in $\mathbb{R}^2$ that represents the location of the center of the $k$th c-site that is attached to both the $i$th and the $j$th cell centers (so, $\mathbf{c}_{i,j,k} = \mathbf{c}_{j,i,k}$). The coordinates will be denoted $\mathbf{c}_{i,j,k} = (x_{i,j,k}, y_{i,j,k})$.

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- Let $n_{i,j}$ denote the number of c-sites connecting the $i$th and the $j$th cell and let $m$ denote the total number of c-sites, so $m = \sum_{i<j} n_{i,j}$.
- The drag coefficients will be denoted $\gamma_i \in (0, \infty)$ for the $i$th cell, $\gamma_{i,j,k} \in (0, \infty)$ for the $k$th c-site between the $i$th and the $j$th cells.

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- Let $f : [0, \infty) \to [0, \infty]$ be a continuously differentiable function, with $f(0) = \infty$, and with support $[0, r]$ for some real number $r > 0$. This function will denote the magnitude of the body force or the force that repels any two cells as soon as their centers become too close to each other (i.e. the distance between the centers of the cells is less than $r$)

# Formulation of the Model

The model is derived from Newton's second Law of motion.
The principal forces acting on the cell are

- the body force (which vanishes when the cell centers are sufficiently far away from each other),
- the forces generated by the c-sites (linear forces), and
- the force of drag which in this environment is proportional to the velocity of the cell, but in the direction opposite the velocity.

So, in general, the equation (for a cell of mass $m$) of motion associated with the cell-system is

$$m\ddot{\mathbf{x}}_i = \sum_{\substack{j=1 \\ j\neq i}}^{n} f(\|\mathbf{x}_i - \mathbf{x}_j\|)\frac{\mathbf{x}_i - \mathbf{x}_j}{\|\mathbf{x}_i - \mathbf{x}_j\|} + \sum_{j=1}^{n}\sum_{k=1}^{n_{i,j}} \alpha(\mathbf{c}_{i,j,k} - \mathbf{x}_i) - \gamma_1 \dot{\mathbf{x}}_i.$$

# Formulation of the Model

Writing an equations for each body, yields the following system:

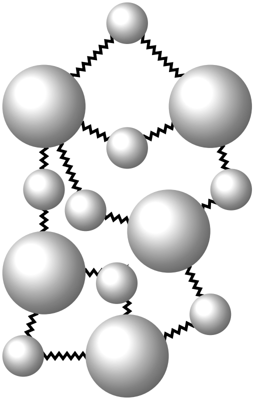
$$\begin{cases} \gamma_1 \dot{\mathbf{x}}_i = & \sum_{\substack{j=1 \\ j \neq i}}^{n} f(\|\mathbf{x}_i - \mathbf{x}_j\|) \frac{\mathbf{x}_i - \mathbf{x}_j}{\|\mathbf{x}_i - \mathbf{x}_j\|} + \sum_{j=1}^{n} \sum_{k=1}^{n_{i,j}} \alpha m_{i,j} (\mathbf{c}_{i,j,k} - \mathbf{x}_1) \\ \gamma_2 \dot{\mathbf{c}}_{i,j,k}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

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

# A Cell System

## Definition

A *cell system* is a connected bipartite graph, together with some additional information associated with elements of the graph. One of the partite groups represents the c-sites, the other, the cells. The c-site partite group is bivalent and incident with no multi-edges. The additional information coupled with the graph is as follows:



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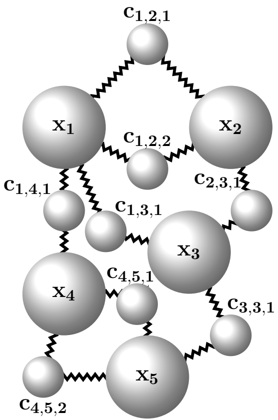
1. The location, on the plane, of each vertex ($\mathbf{x}_i \in \mathbb{R}^2$ for vertices in the cell partite and ($\mathbf{c}_{i,j,k} \in \mathbb{R}^2$ for vertices in the c-site partite).



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3. A function $\mathfrak{a}_{i,j,k,l} : \mathbb{R}^4 \rightarrow \mathbb{R}^2$ associated with each edge modeling the attractive force of the cell and the c-site incident to that edge. The output of $\mathfrak{a}_{i,j,k,l}$ is a scalar multiple of the difference of the arguments being used (according to $l$. Only two of the arguments are ever used at a time).

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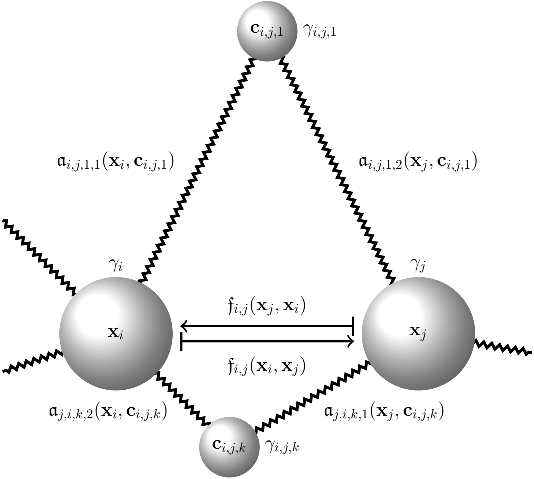
4. A function $\mathfrak{f}_{i,j} : \mathbb{R}^4 \to \mathbb{R}^2$ associated with a pair of vertices in the cell partite group which models the repulsive body force of the cells in the pair.

# A Cell System



# Cell System Model

## Definition

A *cell system model* is an initial value problem (IVP) associated with a cell system formulated this way

$$\begin{cases} \gamma_i \dot{\mathbf{x}}_i = \displaystyle\sum_{j=1}^{n} \mathfrak{f}_{i,j}(\mathbf{x}_i, \mathbf{x}_j) - \sum_{j=1}^{n} \sum_{k=1}^{n_{i,j}} \mathfrak{a}_{i,j,k,1}(\mathbf{x}_i, \mathbf{c}_{i,j,k}) \\ \gamma_{i,j,k} \dot{\mathbf{c}}_{i,j,k} = \mathfrak{a}_{i,j,k,1}(\mathbf{x}_i, \mathbf{c}_{i,j,k}) + \mathfrak{a}_{i,j,k,2}(\mathbf{x}_j, \mathbf{c}_{i,j,k}) \end{cases} \tag{2}$$

Let $\boldsymbol{x} = (\mathbf{x}_1, \ldots, \mathbf{x}_n, \ldots, \mathbf{c}_{i,j,k}, \ldots) \in \mathbb{R}^{2n+2m}$ this is the state variable of the system. Then let $\boldsymbol{f} : \mathbb{R}^{2n+2m} \to \mathbb{R}^{2n+2m}$ such that system (2) may be written as $\dot{\boldsymbol{x}} = \boldsymbol{f}(\boldsymbol{x})$. Here $\boldsymbol{f}$ is said to be a *cell system model force function*. The initial condition will be the state $\boldsymbol{x}^0$ (value of the state variable) of the cell system at some initial time $t_0$.

# Cell System Model

## Definition

So, the cell system model is simply the IVP

$$\begin{cases} \dot{\boldsymbol{x}} = \boldsymbol{f}(\boldsymbol{x}) \\ \boldsymbol{x}(t_0) = \boldsymbol{x}^0. \end{cases}$$

# More Cell Systems

### Definition

A cell system (cell system model) is said to be simple if each pair of cell centers have at most one c-site connecting them, that is $n_{i,j} \leq 1$ for all pairs $i, j = 1, 2, \ldots, n$.

### Definition

A *Hookean cell system* is a cell system in which each

$$\mathfrak{a}_{i,j,k,l}(\mathbf{x}_i, \mathbf{c}_{i,j,k}) = \alpha_{i,j,k}(\mathbf{x}_i - \mathbf{c}_{i,j,k})$$
$$\mathfrak{a}_{i,j,k,2}(\mathbf{x}_j, \mathbf{c}_{i,j,k}) = \alpha_{i,j,k}(\mathbf{x}_j - \mathbf{c}_{i,j,k})$$

this we refer to as the Hookean condition.

# Hookean Cell System, Type 1 and Type 2

## Definition

It will be said to be of *type 1* if

1. each $\gamma_i = \gamma_1$ for $i = 1, 2, \ldots, n$ and each $\gamma_{i,j,k} = \gamma_2$ for each c-site,
2. each
$$\mathfrak{f}_{i,j}(\mathbf{x}_i, \mathbf{x}_j) = f(\|\mathbf{x}_i - \mathbf{x}_j\|)\frac{\mathbf{x}_i - \mathbf{x}_j}{\|\mathbf{x}_i - \mathbf{x}_j\|}$$
for each $i, j = 1, 2, \ldots, n$ ($\mathfrak{f}_{i,i} = 0$) for some $f : [0, \infty) \to [0, \infty]$ with the following properties:
   1. $f(0) = \infty$,
   2. for some $r > 0$, $f$ has support $[0, r]$,
   3. $f$ is $C^1$, convex, and decreasing on $(0, 1)$,

   (In this case $f$ will be referred to as the *generating function*)
3. each $\alpha_{i,j,k} = \alpha m_{i,j}$.

# Hookean Cell System, Type 1 and Type 2

**Definition**

It will be said to be of *type 2* if

1. each $\gamma_i = \gamma_1$ for $i = 1, 2, \ldots, n$ and
2. each $\mathfrak{f}_{i,j}$ is as in the definition of a Hookean cell system of type 1.

Note that all Hookean cell system of type 1 are also type 2.

# Hookean Cell System Models, Type 1 and Type 2

**Definition**

A *Hookean cell system model* is a cell system model associated with a Hookean cell system. And Hookean cell system models of type 1 and 2 are similarly defined according to the Hookean cell systems with which the model is associated.

For convenience a Hookean cell system and its corresponding model will be denoted by the fraktur character $\mathfrak{H}$, and when it is important to vary the initial conditions without changing the underlying differential equation, we will specify the initial conditions by writing $\mathfrak{H}(t_0, \boldsymbol{x}^0)$.

# Center of Drag

## Definition

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

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

## Proposition

*Given a Hookean cell system of type 2, the center of drag is conserved throughout the entire evolution of that system.*

## Bound on Solutions

**Proposition**

*If $\boldsymbol{x}(t)$ is a solution to a Hookean cell system model $\mathfrak{H}$, then there exist an $L > 0$ which depends on $\boldsymbol{x}^0$ such that*

$$\|\boldsymbol{x}(t)\| < L$$

*for all $t$.*

# $\Theta_n$

Let

$$\Theta_n = \{\boldsymbol{x} = (\mathbf{x}_1, \mathbf{x}_2, \ldots, \mathbf{x}_n) \in \mathbb{R}^{2n} : \|\mathbf{x}_i - \mathbf{x}_j\| \neq 0\}$$

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*The set $\Theta_n$ is an invariant set of the ordinary differential equation in any Hookean cell system.*

# $\Theta_{n,\epsilon}$

For $\epsilon > 0$ let

$$\Theta_{n,\epsilon} = \left\{ \boldsymbol{x} = (\mathbf{x}_1, \mathbf{x}_2, \ldots, \mathbf{x}_n) \in \mathbb{R}^{2n} : \|\mathbf{x}_i - \mathbf{x}_j\| > \epsilon 0 \right\}$$

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**Proposition**

*The set $\Theta_{n,\epsilon}$ is open as well as connected.*

**Lemma**

*Given the a Hookean cell system model, $\mathfrak{H}$, there exists an $\epsilon > 0$ for which if there is a solution to $\mathfrak{H}$ it will remain in $\Theta_{n,\epsilon} \times \mathbb{R}^{2m}$.*

# Lipshitz

## Proposition

*For any $\epsilon > 0$ and Hookean cell system model of type 1 $\mathfrak{H}$, the force function $\boldsymbol{f}$ of $\mathfrak{H}$ is Lipshitz on any open ball contained in $\Theta_{n,\epsilon}$.*

Notice, the fact that $\boldsymbol{f}$ is Lipshitz on any open ball in any $\Theta_{n,\epsilon}$ does not depend on the initial condition $\boldsymbol{x}^0$. However, there exists a bound on $\|\boldsymbol{f}(\boldsymbol{x})\|$, and this bound does depend on the initial condition of $\mathfrak{H}$.

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**Lemma**

*Given the a Hookean cell system model, $\mathfrak{H}$, there exists an $N > 0$ such that $N > \|\boldsymbol{f}(\boldsymbol{x})\|$ for all $\boldsymbol{x} \in \Theta_{n,\epsilon} \times \mathbb{R}^{2m}$ and $\|\boldsymbol{x}\| < L$ (where $L$ is given as a bound on a solution $\boldsymbol{x}(t)$ of $\mathfrak{H}$ by a previous proposition).*

# Existence and Uniqueness

**Theorem (Local Existence and Uniqueness for Hookean Cell System Models of Type 2)**

*For any Hookean cell system model of type 2* $\mathfrak{H}$, *there exists a* $\delta > 0$ *such that* $\mathfrak{H}$ *has a unique solution* $\boldsymbol{x}(t)$ *on* $[t_0, t_0 + \delta]$.

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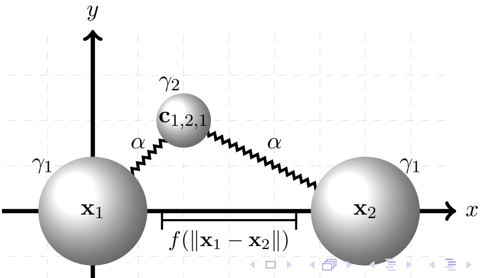
**Theorem (Global Existence and Uniqueness for Hookean Cell System Models of Type 2)**

*Given Hookean cell system model of Type 2 $\mathfrak{H}$ 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

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



# Two Regimes

It is useful to consider the problem in two cases:

Regime 1. $\|\mathbf{x}_2 - \mathbf{x}_1\| \geq r$ (recall $r$ is the smallest value for which $f(r) = 0$). Here the system a linear system in which elementary methods may be used to obtain an explicit solution, which will have to agree with $\boldsymbol{x}$ as far as the cell centers are sufficiently far apart. This case will be described as $\hat{\mathfrak{H}}$ being "beyond the support of $f$."

Regime 2. $\|\mathbf{x}_2 - \mathbf{x}_1\| < r$. In this regime $\hat{\mathfrak{H}}$ is referred to as being "within the support of $f$." Here, $\hat{\mathfrak{H}}$ is possibly non-linear, so the analysis of it will be much different from the analysis of $\hat{\mathfrak{H}}$

# Regime 1: beyond the Support of $f$

In this regime $\hat{\mathfrak{H}}$ may be written with out 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

$$
\begin{aligned}
x_1(t) &= \frac{x_c(0)\gamma_2 + l\gamma_1}{2\gamma_1+\gamma_2} - \frac{l}{2}e^{-\alpha t/\gamma_1} - \frac{2x_c(0)\gamma_2 - l\gamma_2}{2(2\gamma_1+\gamma_2)}e^{-\alpha(\gamma_1^{-1}+2\gamma_2^{-1})t} \\
y_1(t) &= \frac{y_c(0)\gamma_2}{2\gamma_1+\gamma_2} - \frac{y_c(0)\gamma_2}{2\gamma_1+\gamma_2}e^{-\alpha(\gamma_1^{-1}+2\gamma_2^{-1})t} \\
x_2(t) &= \frac{x_c(0)\gamma_2 + l\gamma_1}{2\gamma_1+\gamma_2} + \frac{l}{2}e^{-\alpha t/\gamma_1} - \frac{2x_c(0)\gamma_2 - l\gamma_2}{2(2\gamma_1+\gamma_2)}e^{-\alpha(\gamma_1^{-1}+2\gamma_2^{-1})t} \\
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\end{aligned}
$$

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! Proving that in the linear case (outside of the support of $f$) no rotation occurs between the two cells.

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

Indeed, using the equations above we may relate $y_c$ and $x_c$ in the following way:

$$y_c = x_c \left( \frac{2y_c(0)(2\gamma_1 + \gamma_2)}{2x_c(0) - l} \right) + \left( y_c(0)\gamma_2 - \frac{2x_c(0)y_c(0)\gamma_2 - y_c(0)l\gamma_1}{2x_c(0) - l} \right)$$

And so the c-site travels in a straight line to it's equilibrium position.

# Analysis of the Solution

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

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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 where the cells will be as soon as the body force becomes nonzero.

# Regime 2: Within the Support of $f$

We analyze this nonlinear system in two steps.

1. The set of equilibria for the system is identified and studied and the stability of the equilibria is explored. In this discussion of the equilibria initial conditions have no bearing, so rather then talking in terms of $\hat{\mathfrak{H}}$, it is discussed in terms of $\boldsymbol{f}$, the force function of $\hat{\mathfrak{H}}$.
2. The second step includes a method for finding explicit solutions is discussed by proposing guesses based on our analysis of the system in regime one. The existence and uniqueness theorem then establishes the guesses as the unique solution to $\hat{\mathfrak{H}}$.

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

Substituting this for **c** into the first and second equations reduces the system to

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

or more simply

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

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

And so,

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

if $\Delta x = \|\mathbf{x}_1 - \mathbf{x}_2\|$. So, we become interested in the fixed point(s) of $\frac{2}{\alpha} f$. It can be shown that $\frac{2}{\alpha} f$ has a unique fixed point; let $r_0$ be that point. We then arrive to both necessary and sufficient conditions for the critical points of our system and the critical points of this system are all the points $\boldsymbol{x} \in \mathbb{R}^6$ such that

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

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

## 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

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

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

These partials taken at some point $(x_a, y_a, \theta)$ 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 $G_\theta$ the basis of the tangent space of $c(\boldsymbol{f})$ at some point $(x_a, y_a, \theta)$ 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

To analysis the stability of a fixed point $\tilde{\boldsymbol{x}}$ define the point $\boldsymbol{y} \in \mathbb{R}^6$ by $\boldsymbol{y} = \boldsymbol{x} - \tilde{\boldsymbol{x}}$. So, $\boldsymbol{x} = \boldsymbol{y} + \tilde{\boldsymbol{x}}$ and $\dot{\boldsymbol{x}} = \boldsymbol{f}(\boldsymbol{x})$ becomes $\dot{\boldsymbol{y}} = \boldsymbol{f}\left(\boldsymbol{y} + \tilde{\boldsymbol{x}}\right)$. Using a Taylor expansion provides

$$\begin{aligned} \dot{\boldsymbol{y}} &= \boldsymbol{f}(\tilde{\boldsymbol{x}}) + \mathbf{Df}(\tilde{\boldsymbol{x}})\boldsymbol{y} + \mathcal{O}\left(\|\boldsymbol{y}\|^2\right) \\ &= \mathbf{Df}(\tilde{\boldsymbol{x}})\boldsymbol{y} + \mathcal{O}\left(\|\boldsymbol{y}\|^2\right). \end{aligned}$$

So, it is sufficient to determine the dynamics of $\boldsymbol{y}$ close to $\mathbf{0}$. For this we look at the linear part, $\mathbf{Df}(\tilde{\boldsymbol{x}})\boldsymbol{y}$. Before taking the derivative of $\boldsymbol{f}$ at $\tilde{\boldsymbol{x}}$ it may be helpful to express $\boldsymbol{f}(\boldsymbol{x})$ like this:

$$\boldsymbol{f}(\boldsymbol{x}) = \begin{pmatrix} \left(g - \frac{\alpha}{\gamma_1}\right) x_1 - g x_2 + \frac{\alpha}{\gamma_1} x_c \\ \left(g - \frac{\alpha}{\gamma_1}\right) y_1 - g y_2 + \frac{\alpha}{\gamma_1} y_c \\ -g x_1 + \left(g - \frac{\alpha}{\gamma_1}\right) x_2 + \frac{\alpha}{\gamma_1} x_c \\ -g y_1 + \left(g - \frac{\alpha}{\gamma_1}\right) y_2 + \frac{\alpha}{\gamma_1} y_c \\ \frac{\alpha}{\gamma_2} x_1 + \frac{\alpha}{\gamma_2} x_2 - \frac{2\alpha}{\gamma_2} x_c \\ \frac{\alpha}{\gamma_2} y_1 + \frac{\alpha}{\gamma_2} y_2 - \frac{2\alpha}{\gamma_2} y_c \end{pmatrix}.$$

# The Stability of the equilibria

So, then $\mathbf{Df}(\tilde{\boldsymbol{x}})$ 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 $\mathbf{Df}(\tilde{\boldsymbol{x}})$ 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 because $\theta$ from the parameterization of $c(\boldsymbol{f})$ by $G$ was defined to be the angle from the positive $x$-axis the solution was rotated counterclockwise, $\frac{y_1-y_2}{x_1-x_2} = \tan\theta$.

# The Stability of the equilibria

So, both the center manifold and the set of equilibria of $\dot{\boldsymbol{x}} = \boldsymbol{f}(\boldsymbol{x})$ are one and the same. Since all of the nonzero eigenvalues of $\mathbf{Df}(\tilde{\boldsymbol{x}})$ are negative, there is no unstable manifold.

# The solution to $\hat{\mathfrak{H}}$

The system $\hat{\mathfrak{H}}$ is given below, where $l > 0$ and $y_c(0) \geq 0$

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

By Theorem 20 there exists a unique solution to $\hat{\mathfrak{H}}$ on $[0, \infty)$. let $\tilde{\boldsymbol{x}}(t) = (\tilde{x}_1(t), \tilde{y}_1(t), \tilde{x}_2(t), \tilde{y}_2(t), \tilde{x}_c(t), \tilde{y}_c(t))$ be that solution.

# The solution to $\hat{\mathfrak{H}}$

let $g(x_1, x_2, y_1, y_2) = f(\|\mathbf{x}_1 - \mathbf{x}_2\|)/\|\mathbf{x}_1 - \mathbf{x}_2\|$. Expand (46) by writing the equation for each component of the vectors $\mathbf{x}_1$, $\mathbf{x}_2$, and $\mathbf{c}$. This produces an equivalent system of six equations together with initial conditions.

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

# The solution to $\hat{\mathfrak{H}}$

Now, we make a shrewd guess.

- $y_1(t) = y_2(t) =: y(t)$
-

$$\gamma_1 x_1(t) + \gamma_1 x_2(t) + \gamma_2 x_c(t) 2\gamma_1 + \gamma_2 = \frac{x_c(0)\gamma_2 + l\gamma_1}{2\gamma_1 + \gamma_2}. \quad (3)$$

As it turns out this is enough to simplify the system down to actually computing a solution.

# The solution to $\hat{\mathfrak{H}}$

- $x_1(t)$ 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

In order to state the theorem more concisely we define a specific projection transformation: let $P_{n,m} : \mathbb{R}^{2n+2m} \to \mathbb{R}^{2n}$ be defined for $\boldsymbol{x} = (\mathbf{x}_1, \mathbf{x}_2, \ldots, \mathbf{x}_n, \mathbf{c}_1, \mathbf{c}_2, \ldots, \mathbf{c}_m)^T \in \mathbb{R}^{2n+2m}$ as

$$P_{n,m}(\boldsymbol{x}) = (\mathbf{x}_1, \mathbf{x}_2, \ldots, \mathbf{x}_n)^T.$$

# C-site Reduction Theorem for Two Cells

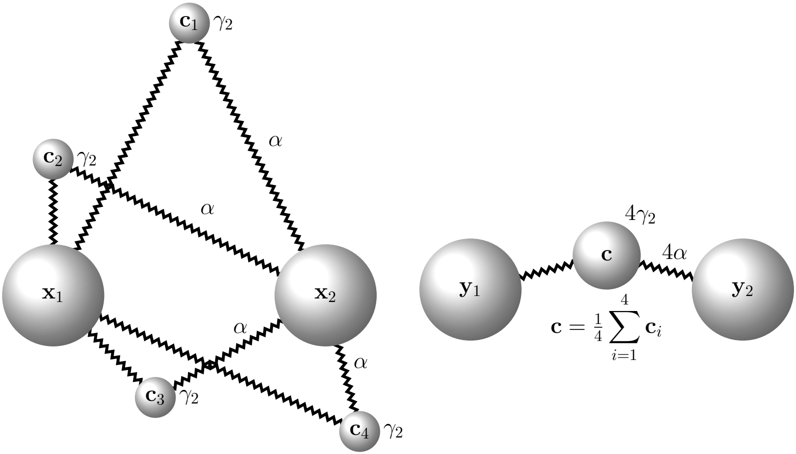
## Theorem (c-Site Reduction Theorem)

*Let $\mathfrak{H}$ be a Hookean cell system model of type 1 with two cells and $m$ c-sites, $\boldsymbol{x}^0 \in \Theta_n \times \mathbb{R}^{2m}$, and $\boldsymbol{x}(t)$ be the solution to $\mathfrak{H}(0, \boldsymbol{x}^0)$, Then there exist a Hookean cell system model of type 2, $\mathfrak{H}'$, with two cells and one c-site, such that if $\boldsymbol{y}(t)$ is a solution to $\mathfrak{H}'$,*

$$P_{2,m}(\boldsymbol{x}(t)) = P_{2,1}(\boldsymbol{y}(t)) \qquad \text{for all } t \in [0, \infty).$$

*Furthermore, the drag coefficient of the c-site is $m\gamma_2$, the pseudopodia spring constants are $m\alpha$ and the location of the center of the c-site is $\mathbf{c}(t) = \frac{1}{m}\sum_{i=1}^{m} \mathbf{c}_i(t)$.*

# C-site Reduction Theorem for Two Cells



# Consequences of C-site Reduction Theorem for Two Cells

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

# Consequences of C-site Reduction Theorem for Two Cells

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

$$
\mathbf{c}_j(t) = \begin{pmatrix}
\left(x_{cj}(0) - \frac{1}{m}\sum_{i=1}^{m} x_{ci}(0)\right) e^{-2\frac{\alpha}{\gamma_2}t} + \left(-\frac{\gamma_1 l}{m\gamma_2 + 2\gamma_1} + \frac{2\gamma_1}{m(m\gamma_2+2\gamma_1)}\sum_{i=1}^{m} x_{ci}(0)\right) e^{-\left(2\frac{\alpha}{\gamma_2} + m\frac{\alpha}{\gamma_1}\right)} \\
\left(y_{cj}(0) - \frac{1}{m}\sum_{i=1}^{m} y_{ci}(0)\right) e^{-2\frac{\alpha}{\gamma_2}t} + \left(\frac{2\gamma_1}{m(m\gamma_2+2\gamma_1)}\sum_{i=1}^{m} y_{ci}(0)\right) e^{-\left(2\frac{\alpha}{\gamma_2} + m\frac{\alpha}{\gamma_1}\right)}
\end{pmatrix}
$$

# General C-site Reduction Theorem

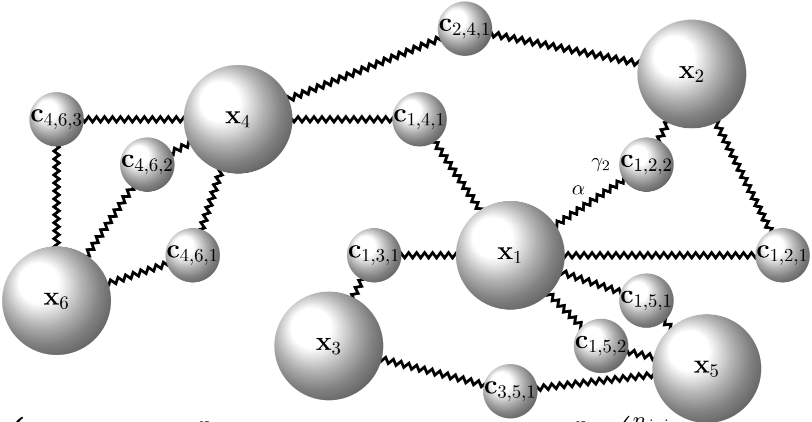
## Theorem (General c-Site Reduction Theorem)

*Let* $\mathfrak{H}$ *be a Hookean cell system model of type 1 with* $n$ *cells and* $m$ *c-sites,* $\boldsymbol{x}^0 \in \Theta_n \times \mathbb{R}^{2m}$*, and* $\boldsymbol{x}(t)$ *be the solution to* $\mathfrak{H}(0, \boldsymbol{x}^0)$*, Then there exist a Hookean cell system model of type 2,* $\mathfrak{H}'$*, with* $n$ *cells and* $m' = \sum_{i<j} m_{i,j}$ *c-site, such that if* $\boldsymbol{y}(t)$ *is a solution to* $\mathfrak{H}'$*,*

$$P_{n,m}(\boldsymbol{x}(t)) = P_{n,m'}(\boldsymbol{y}(t)) \qquad \text{for all } t \in [0, \infty).$$

*In the cell system which generates* $\mathfrak{H}'$*, each of the* $m'$ *c-sites connects a unique pair of cells* $\mathbf{x}_i$ *and* $\mathbf{x}_j$*, these will be referred to as* $\mathbf{c}_{i,j}$*. The drag coefficient* $\gamma_{i,j}$ *of* $\mathbf{c}_{i,j}$ *is* $n_{i,j}\gamma_2$*, the pseudopodia spring constants are* $\alpha_{i,j} = n_{i,j}\alpha$ *and the location of the center of the c-site is* $\mathbf{c}_{i,j}(t) = \frac{1}{n_{i,j}} \sum_{k=1}^{n_{i,j}} \mathbf{c}_{i,j,k}(t)$*.*

# General C-site Reduction Theorem




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

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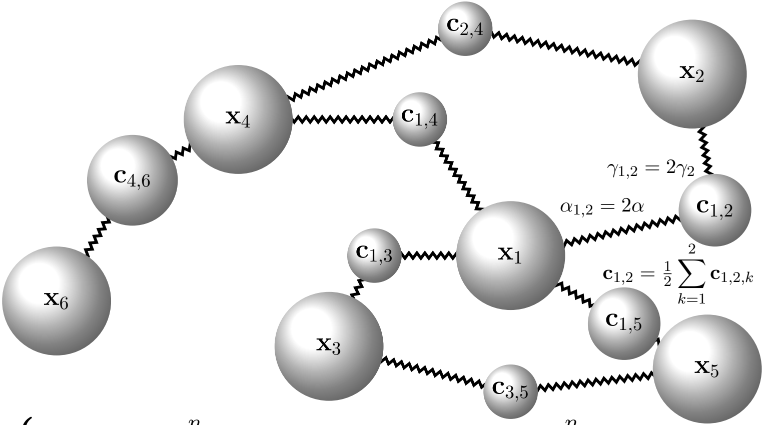


$$\begin{cases} \gamma_1 \dot{\boldsymbol{x}}_j = \sum_{i=1}^{n} f(\|\boldsymbol{x}_j - \boldsymbol{x}_i\|) \dfrac{\boldsymbol{x}_j - \boldsymbol{x}_i}{\|\boldsymbol{x}_j - \boldsymbol{x}_i\|} + \sum_{i=1}^{n} \alpha n_{i,j} (\boldsymbol{c}_{i,j} - \boldsymbol{x}_j) \\ \gamma_2 n_{i,j} \dot{\boldsymbol{c}}_{i,j}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

# 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?

# Reformulation of the Model

$$\left\{ \begin{aligned} \gamma_1 \dot{\mathbf{x}}_j = & \sum_{i=1}^{n} \frac{f(\|\mathbf{x}_j - \mathbf{x}_i\|)}{\|\mathbf{x}_i - \mathbf{x}_j\|} (\mathbf{x}_i - \mathbf{x}_j) + \sum_{i=1}^{n} \alpha_{i,j} (\mathbf{c}_{i,j} - \mathbf{x}_j) \\ \gamma_{i,j} \dot{\mathbf{c}}_{i,j} = & \alpha_{i,j} (\mathbf{x}_i + \mathbf{x}_j - 2\mathbf{c}_{i,j}). \end{aligned} \right. \tag{4}$$

# Reformulation of the Model

$$\left\{ \begin{array}{rl} \gamma_1 \dot{\mathbf{x}}_j = & \sum_{i=1}^{n} \frac{f(\|\mathbf{x}_j - \mathbf{x}_i\|)}{\|\mathbf{x}_i - \mathbf{x}_j\|}(\mathbf{x}_i - \mathbf{x}_j) + \sum_{i=1}^{n} \alpha_{i,j}(\mathbf{c}_{i,j} - \mathbf{x}_j) \\ \gamma_{i,j}\dot{\mathbf{c}}_{i,j} = & \alpha_{i,j}(\mathbf{x}_i + \mathbf{x}_j - 2\mathbf{c}_{i,j}). \end{array} \right. \tag{4}$$

As usual we let
$\boldsymbol{x} = (\mathbf{x}_1, \ldots, \mathbf{x}_n, \ldots, \mathbf{c}_{i,j}, \ldots)^T$

# Reformulation of the Model

To find the critical values of this system we shall set each left hand side to zero. Now for each c-site equation for which $m_{i,j} \neq 0$ we may solve for $\mathbf{c}_{i,j}$ achieving

$$\mathbf{c}_{i,j} = \frac{\boldsymbol{x}_i + \boldsymbol{x}_j}{2}.$$

Substituting these into the cell equations for any $i$ and $j$ such that $m_{i,j} \neq 0$ we get

$$\begin{aligned} 0 &= \sum_{i=1}^{n} \frac{f(\|\mathbf{x}_j - \mathbf{x}_i\|)}{\|\mathbf{x}_i - \mathbf{x}_j\|}(\mathbf{x}_i - \mathbf{x}_j) + \sum_{i=1}^{n} m_{i,j}\alpha_{i,j}\left(\frac{\boldsymbol{x}_i - \boldsymbol{x}_j}{2}\right) \\ &= \sum_{i=1}^{n}\left(\frac{f(\|\mathbf{x}_i - \mathbf{x}_j\|)}{\|\mathbf{x}_i - \mathbf{x}_j\|} - \frac{m_{i,j}\alpha_{i,j}}{2}\right)(\boldsymbol{x}_j - \boldsymbol{x}_i) \end{aligned}$$

let

$$\beta_{i,j} := \frac{f(\|\mathbf{x}_i - \mathbf{x}_j\|)}{\|\mathbf{x}_i - \mathbf{x}_j\|} - \frac{m_{i,j}\alpha_{i,j}}{2}$$

and define $\beta_{j,j} = 0$. Notice, $\beta_{i,j} = \beta_{j,i}$.

# Reformulation of the Model

So, our equations become for any $j = 1, 2, \ldots, n$

$$\begin{aligned} 0 &= \sum_{i=1}^{n} \beta_{i,j}(\boldsymbol{x}_j - \boldsymbol{x}_i) \\ &= \sum_{i=1}^{n} \beta_{i,j}\boldsymbol{x}_j - \sum_{i=1}^{n} \beta_{i,j}\boldsymbol{x}_i \\ &= -\beta_{1,j}\boldsymbol{x}_1 - \beta_{2,j}\boldsymbol{x}_2 - \cdots - \beta_{j-1,j}\boldsymbol{x}_{j-1} + \sum_{i=1}^{n} \beta_{i,j}\boldsymbol{x}_j - \beta_{j+1,j}\boldsymbol{x}_{j+1} - \cdots - \beta_{n,j}\boldsymbol{x}_n \end{aligned}$$

# Reformulation of the Model

this gives us the system

$$\begin{cases} 0 = & -\sum_{i=1}^{n}\beta_{i,1}\boldsymbol{x}_1 & + & \beta_{2,1}\boldsymbol{x}_2 & + & \beta_{3,1}\boldsymbol{x}_3 & + & \dots & + & \beta_{n,1}\boldsymbol{x}_n \\ 0 = & \beta_{1,2}\boldsymbol{x}_1 & - & \sum_{i=1}^{n}\beta_{i,2}\boldsymbol{x}_2 & + & \beta_{3,1}\boldsymbol{x}_3 & + & \dots & + & \beta_{n,2}\boldsymbol{x}_n \\ 0 = & \beta_{1,3}\boldsymbol{x}_1 & + & \beta_{2,3}\boldsymbol{x}_2 & - & \sum_{i=1}^{n}\beta_{i,3}\boldsymbol{x}_3 & + & \dots & + & \beta_{n,3}\boldsymbol{x}_n \\ & & & & \vdots & & & & & \\ 0 = & \beta_{1,n}\boldsymbol{x}_1 & + & \beta_{2,n}\boldsymbol{x}_2 & + & \beta_{3,n}\boldsymbol{x}_3 & + & \dots & - & \sum_{i=1}^{n}\beta_{i,n}\boldsymbol{x}_n \end{cases}$$

# Reformulation of the Model

which may be written in matrix form if

$$B = \begin{pmatrix} -\sum_{i=1}^{n} \beta_{i,1} & \beta_{2,1} & \beta_{3,1} & \cdots & \beta_{n,1} \\ \beta_{1,2} & -\sum_{i=1}^{n} \beta_{i,2} & \beta_{3,1} & \cdots & \beta_{n,2} \\ \beta_{1,3} & \beta_{2,3} & -\sum_{i=1}^{n} \beta_{i,3} & \cdots & \beta_{n,3} \\ \vdots & \vdots & \vdots & \ddots & \vdots \\ \beta_{1,n} & \beta_{2,n} & \beta_{3,n} & \cdots & -\sum_{i=1}^{n} \beta_{i,n} \end{pmatrix}$$

# Reformulation of the Model

(that is a capital beta) and

$$\boldsymbol{x}_n = \begin{pmatrix} \mathbf{x}_1 \\ \vdots \\ \mathbf{x}_n \end{pmatrix} \in \mathbb{R}^{2n}$$

as

$$0 = B\boldsymbol{x}_n$$

# The behavior of the system at that equilibria

To study the stability of the equilibria we have shown by an example that center manifold theory may be employed and that the set of all equilibria itself formed the center manifold. This find was facilitated by the fact that the set of all equilibria could be defined explicitly. It would be interesting to see if such is the case in systems with a greater number of cells.
Another approach may be to suppose that a point is an equilibria and compute the derivative matrix at that point to determine the tangent space of the center manifold (assume there is one, which is likely because there is sure to be a continuum of equilibria). This may then give information of the set of equilibira.

# The next step in modifying the model to make it a closer approximation of the motion of a slug

After a firm understand of how these cell systems behave in a deterministic scene the next step would be to include random switching times that govern the attachment and detachment of the c-sites from the cells.

# Stochastics in this frame work

Let $(\Omega, \mathbb{H}, \mathbb{P})$ be a probability space. And let $\psi$ be a Bernoulli random variable. The *state* of a c-site describes whether or not it is "attached" or "detached." A c-site is said to be *attached* if it is connected to two cells and *detached* if otherwise. In the model the random variable $\psi$ determines the state of the c-site. If $\psi = 1$ the c-site is attached to both of the cells if $\psi = 0$ the c-site is detached.

$$\begin{cases} \gamma_i \dot{\mathbf{x}}_i = \displaystyle\sum_{j=1}^{n} \mathfrak{f}_{i,j}(\mathbf{x}_i, \mathbf{x}_j) - \sum_{j=1}^{n} \sum_{k=1}^{n_{i,j}} \psi_{i,j,k,1} \mathfrak{a}_{i,j,k,1}(\mathbf{x}_i, \mathbf{c}_{i,j,k}) \\ \psi_{i,j,k} \gamma_{i,j,k} \dot{\mathbf{c}}_{i,j,k} = \psi_{i,j,k,1} \mathfrak{a}_{i,j,k,1}(\mathbf{x}_i, \mathbf{c}_{i,j,k}) + \psi_{i,j,k,2} \mathfrak{a}_{i,j,k,2}(\mathbf{x}_j, \mathbf{c}_{i,j,k}) \end{cases} \tag{5}$$