Chapter 1

Biophysical modelling of rod-shaped bacterial cells

1.1 Biophysical model

The measurements of individual cells in microcolonies of *E. coli* presented above are consistent with the overview presented by Koch [**?**] that cells have fixed diameter and grow only along their major axis, and the findings of Wang *et al.* [**?**] showing that cells are equally bisected on division. The observation that cell diameter is constant suggests that cells are *rigid* except in the direction of their growth axis. Following this suggestion, we formulated a simple model of cellular growth on an agar substrate as follows:

1. Cells are rigid elongating capsules [**?**].
2. Viscous drag dominates inertia; cells are non-motile and move only when subjected to a force [**?**].
3. The distribution of cell lengths at division is constant, and each cell divides in half [**?**, **?**].
4. Each cell's unconstrained growth rate is proportional to its length [**?**].
5. Growth is constrained by forces between cells and from viscous drag from the substrate (figure 1.1). The ratio of the work required to constrain growth to the work required to move a cell is defined by a parameter Γ.

In a rigid body mechanics model objects cannot be deformed and are completely represented by their position and orientation. We extend this formulation by allowing cell length to vary, adding an extra degree of freedom to accommodate growth.

1.2 Mathematical description of biophysical model

1.2.1 Motion of cells due to applied impulse

Bacterial cells are modelled as capsule-shaped rigid bodies, that is cylinders capped with hemispherical ends. Each cell is represented by its position, orientation and length ($\mathbf{x}$, θ, l), and the associated linear, angular, and growth velocity ($\mathbf{v}_{\text{lin}}$, $\mathbf{w}$, v_{growth}). Here v_{growth} is the linear growth rate dl/dt. By extension of the usual rigid-body formulation, we define the generalised position of a cell as $\tilde{\mathbf{x}} = \begin{pmatrix} \mathbf{x} & \theta & l \end{pmatrix}^T$, and the generalised velocity as $\tilde{\mathbf{v}} = d\tilde{\mathbf{x}}/dt = \begin{pmatrix} \mathbf{v}_{\text{lin}} & \mathbf{w} & v_{\text{growth}} \end{pmatrix}^T$. Similarly there is a generalised momentum associated with the motion of the cell $\tilde{\mathbf{p}} = \begin{pmatrix} \mathbf{p} & \mathbf{L} & g \end{pmatrix}^T$, with linear, angular and growth components. Cells grow by acquiring growth momentum g which causes extension in length. For a physically possible arrangement of

cells, this extension in length cannot cause the cells to overlap or intersect, leading to a system of constraints. It is the solution of this system of constraints, which is derived below, that results in computation of the correct arrangement of cells during colony growth.

In appendix A I show with the assumptions listed above, under a generalised impulse $\Delta\tilde{\mathbf{p}}_i$ the change in generalised position of a cell $\Delta\tilde{\mathbf{x}}_i$ is determined by a matrix $\mathbf{M}_i$ such that:

$$\Delta\tilde{\mathbf{x}}_i = {\mathbf{M_i}}^{-1}\Delta\tilde{\mathbf{p}}_i \tag{1.1}$$

$$= \begin{bmatrix} \text{diag}(\frac{1}{\mu l_0}) & 0 & 0 \\ 0 & \frac{12\mathbf{P_i}}{\mu l_0^3} & 0 \\ 0 & 0 & \frac{1}{\gamma} \end{bmatrix} \begin{bmatrix} \Delta\mathbf{p}_i \\ \Delta\mathbf{L}_i \\ \Delta g_i \end{bmatrix} \tag{1.2}$$

where l_0 is the length of cell i, and ${\mathbf{M_i}}^{-1}$ is written in block form - $\text{diag}(\frac{1}{\mu l_0})$ and $\frac{12\mathbf{P}}{\mu l_0^3}$ are (3×3), and $\frac{1}{\gamma}$ is (1×1). The matrix $\mathbf{P}$ is the projection onto the plane perpendicular to the cell axis $\hat{\mathbf{a}}$, i.e. $\mathbf{P}\Delta\mathbf{L} \equiv \Delta\mathbf{L} - \hat{\mathbf{a}}(\hat{\mathbf{a}}\cdot\Delta\mathbf{L})$.

Note. *There are 7 degrees of freedom for each cell, hence generalised position, velocity and impulse are* 7×1 *vectors. There are 3 components of centroid position/velocity/impulse (*$\mathbf{x}$*,* $\mathbf{v}_{\text{lin}}$*,* $\Delta\mathbf{p}$*), 3 components of angular position/velocity/impulse (*θ*,* $\mathbf{w}$*,* $\Delta\mathbf{L}$*), and 1 component of length/growth rate/growth impulse (*l*,* v_{growth}*,* g*).*

1.2.2 Motion of points on cell surfaces

We described above the change in generalised position of a cell due to a generalised impulse, that is the change in its centroid location, angular orientation, and length. Now consider the motion of a point on the surface of this cell due to the change in generalised position. This point is positioned according to vector $\mathbf{q}$ from the center of the capsule $\mathbf{x}_i$, which has axis $\hat{\mathbf{a}}_i$. Its original position is $\mathbf{q}_w = \mathbf{x}_i + \mathbf{q}$. For small displacments the cell axis $\hat{\mathbf{a}}_i$, the associated projection matrix $\mathbf{P}_i$, and the cell length l_0 remain approximately constant, and

$$\Delta\mathbf{q}_w \approx \Delta\mathbf{x_i} + (\Delta\theta_\mathbf{i}\times\mathbf{q}) + \frac{\Delta l_i}{l_0}(\hat{\mathbf{a}}_i\cdot\mathbf{q})\,\hat{\mathbf{a}}_i$$

And substituting from equation A.5:

$$\begin{aligned}\Delta\mathbf{q}_w &\approx \Delta\mathbf{x_i} - (\mathbf{q}\times\Delta\theta_\mathbf{i}) + \frac{(\hat{\mathbf{a}}_i\cdot\mathbf{q})\,\hat{\mathbf{a}}_i}{l_0}\Delta l_i \\ &\approx \frac{1}{\mu l_0}\Delta\mathbf{p}_i - (\mathbf{q}\times\frac{12\mathbf{P}_i}{\mu l_0^3}\Delta\mathbf{L}_i) + \frac{(\hat{\mathbf{a}}_i\cdot\mathbf{q})\,\hat{\mathbf{a}}_i}{l_0}\frac{\Delta g_i}{\gamma}\end{aligned}$$

Now project this vector along the direction vector $\hat{\mathbf{n}}$ of interest to get the position change in a particular direction:

$$\begin{aligned}\Delta q_{\hat{\mathbf{n}}} &= \hat{\mathbf{n}}\cdot\left(\frac{1}{\mu l_0}\Delta\mathbf{p}_i - (\mathbf{q}\times\frac{12\mathbf{P}_i}{\mu l_0^3}\Delta\mathbf{L}_i) + \frac{(\hat{\mathbf{a}}_i\cdot\mathbf{q})\,\hat{\mathbf{a}}_i}{l_0}\frac{\Delta g_i}{\gamma}\right) \\ &= \frac{1}{\mu l_0}\hat{\mathbf{n}}\cdot\Delta\mathbf{p}_i - \frac{12}{\mu l_0^3}(\hat{\mathbf{n}}\times\mathbf{q})\cdot\mathbf{P}_i\Delta\mathbf{L}_i + \frac{(\hat{\mathbf{n}}\cdot\hat{\mathbf{a}}_i)\,(\hat{\mathbf{q}}\cdot\hat{\mathbf{a}}_i)}{l_0}\frac{\Delta g_i}{\gamma}\end{aligned}$$

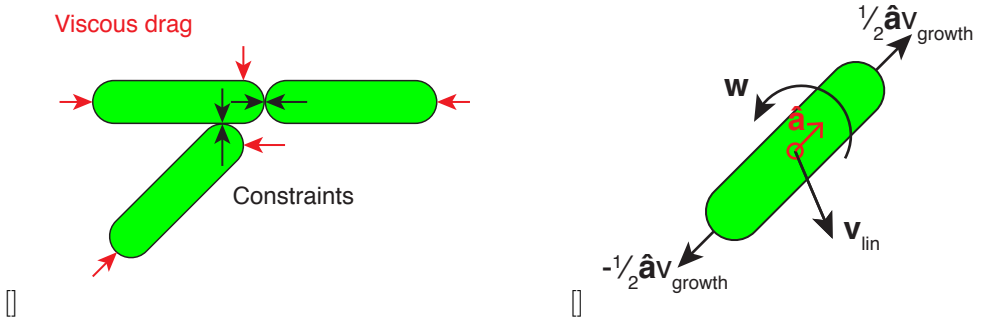

Figure 1.1: **Biophysical model of rod-shaped bacteria, forces and motion.** Biophysical model of rod-shaped bacteria considers each cell as a capsule (shown in two-dimensions). Forces on each cell (a) are generated by viscous drag (red) and constraints at cell-cell contacts (black). The velocity of a point on a cell consists of multiple components (b): the cell centre of mass (red circle) moves with linear velocity $\mathbf{v}_{\text{lin}}$, the cell rotates with angular velocity $\mathbf{w}$, and grows at instantaneous linear rate v_{growth} causing all points to move away from the centre of mass along the axis ($\hat{\mathbf{a}}$).

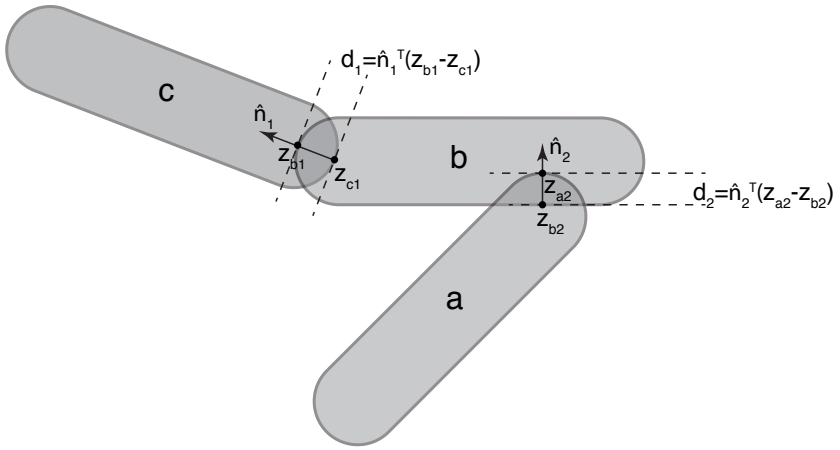

Figure 1.2: .

Which can be written in block matrix form as:

$$\Delta q_{\hat{\mathbf{n}}} = \begin{bmatrix} \hat{\mathbf{n}}^{\mathrm{T}} & -(\hat{\mathbf{n}} \times \mathbf{q})^{\mathrm{T}} & \frac{(\hat{\mathbf{n}}\cdot\hat{\mathbf{a}}_i)(\mathbf{q}\cdot\hat{\mathbf{a}}_i)}{l_0} \end{bmatrix} \begin{bmatrix} \frac{1}{\mu l_0} & 0 & 0 \\ 0 & \frac{12\mathbf{P}_i}{\mu l_0^3} & 0 \\ 0 & 0 & \frac{1}{\gamma} \end{bmatrix} \begin{bmatrix} \Delta\mathbf{p}_i \\ \Delta\mathbf{L}_i \\ \Delta g_i \end{bmatrix}$$

$$= \mathbf{B}_{\hat{\mathbf{n}},\mathbf{q},i}\mathbf{M}_i^{-1}\Delta\tilde{\mathbf{p}}_i$$

Here $\mathbf{B}_{\hat{\mathbf{n}},\mathbf{q},i}$ is a matrix which represents the geometric effect of a generalised position change on a point at $\mathbf{q}$ from the centre of cell i along direction $\hat{\mathbf{n}}$, and matrix $\mathbf{M}_i^{-1}$ is the inverse drag matrix for cell i. The expression for $\Delta q_{\hat{\mathbf{n}}}$ represents the motion of the surface point at position $\mathbf{q}$ relative to the capsule centre in the direction $\hat{\mathbf{n}}$ that results from application of generalised impulse $\Delta\tilde{\mathbf{p}}$. This quantity is central to the formation of the constraints explained below.

1.2.3 Effect of a set of applied impulses on cell-cell overlap distances

Now consider two overlapping capsules a and b, forming contact k. We find the contact points on each cell $\mathbf{z}_{ak}$ and $\mathbf{z}_{bk}$ as described above (figure 1.2). The change in overlap distance d_k is the difference in the movement of these contact points along the contact normal $\hat{\mathbf{n}}_k$. That is for generalised impulses $\Delta\tilde{\mathbf{p}}_a$ and $\Delta\tilde{\mathbf{p}}_b$ applied to cell a and b,

$$\mathbf{B}_{ak}\mathbf{M}_a^{-1}\Delta\tilde{\mathbf{p}}_a - \mathbf{B}_{bk}\mathbf{M}_b^{-1}\Delta\tilde{\mathbf{p}}_b = \Delta d_k$$

where $\mathbf{B}_{ak}$ and $\mathbf{B}_{bk}$ are as $\mathbf{B}$ matrices as defined above using the contact normal $\hat{\mathbf{n}}_k$ as the direction vector, and the relative positions of $\mathbf{z}_{ak}$ and $\mathbf{z}_{bk}$ from their respective cells. Viewed in block matrix form:

$$\begin{bmatrix} \mathbf{B}_{ak}\mathbf{M}_a^{-1} & -\mathbf{B}_{bk}\mathbf{M}_b^{-1} \end{bmatrix} \begin{bmatrix} \Delta\tilde{\mathbf{p}}_a \\ \Delta\tilde{\mathbf{p}}_b \end{bmatrix} = \begin{bmatrix} \Delta d_k \end{bmatrix}$$

In a system of multiple cells, there will be one such equation for each contact k between two capsules. To solve all these equations simultaneously, each equation becomes a row in a matrix equation. For example, with four cells and three contacts, the system might be:

$$\begin{bmatrix} \mathbf{B}_{a1}\mathbf{M}_1^{-1} & -\mathbf{B}_{b1}\mathbf{M}_2^{-1} & 0 & 0 \\ \mathbf{B}_{a2}\mathbf{M}_1^{-1} & 0 & -\mathbf{B}_{c2}\mathbf{M}_3^{-1} & 0 \\ 0 & \mathbf{B}_{b3}\mathbf{M}_1^{-1} & 0 & -\mathbf{B}_{d3}\mathbf{M}_4^{-1} \end{bmatrix} \begin{bmatrix} \Delta\tilde{\mathbf{p}}_a \\ \Delta\tilde{\mathbf{p}}_b \\ \Delta\tilde{\mathbf{p}}_c \\ \Delta\tilde{\mathbf{p}}_d \end{bmatrix} = \begin{bmatrix} \Delta d_1 \\ \Delta d_2 \\ \Delta d_3 \end{bmatrix}$$

$$\begin{bmatrix} \mathbf{B}_{a1} & -\mathbf{B}_{b1} & 0 & 0 \\ \mathbf{B}_{a2} & 0 & -\mathbf{B}_{c2} & 0 \\ 0 & \mathbf{B}_{b3} & 0 & -\mathbf{B}_{d3} \end{bmatrix} \begin{bmatrix} \mathbf{M}_1^{-1} & 0 & 0 & 0 \\ 0 & \mathbf{M}_2^{-1} & 0 & 0 \\ 0 & 0 & \mathbf{M}_3^{-1} & 0 \\ 0 & 0 & 0 & \mathbf{M}_1^{-1} \end{bmatrix} \begin{bmatrix} \Delta\tilde{\mathbf{p}}_a \\ \Delta\tilde{\mathbf{p}}_b \\ \Delta\tilde{\mathbf{p}}_c \\ \Delta\tilde{\mathbf{p}}_d \end{bmatrix} = \begin{bmatrix} \Delta d_1 \\ \Delta d_2 \\ \Delta d_3 \end{bmatrix}$$

and writing the system with single collected matrices and vectors,

$$\mathbf{B}\mathbf{M}^{-1}\Delta\tilde{\mathbf{p}} = \Delta\mathbf{d}$$

Note. *The elements $\mathbf{B}_{ij}\mathbf{M}_i^{-1}$ are computed by the `to_ents` (positive) and `fr_ents` (negative) arrays (7×1 vectors stored in `float8`) which are stored for each cell for each contact it is involved in. We consider contacts to be directed from low to high index, and so only the cell with the lowest index in each contact stores and calculates these entries.*

Note. *In the analysis above I have split the matrices $\mathbf{B}$ and $\mathbf{M}^{-1}$, but currently the combination $\mathbf{B}\mathbf{M}^{-1}$ is computed. It may be better to split it so that we can more easily compute other forms of $\mathbf{B}$, e.g. for adhesion (see below). Application of $\mathbf{M}^{-1}$ is already implemented by `compute_Minvx`.*

1.2.4 Growth of cells generates impulses to prevent overlap

Growth of cells during a discrete time-step Δt is modelled by simply increasing the length of each cell by $v_{\text{growth}}\Delta t$. This causes cells to overlap (figure 1.2). For a physically correct arrangement of cells, reaction or constraint forces must be generated to eliminate this overlap.

A capsule of total length l and radius r is defined as the locus of points within a radius r of the line segment of length $l - 2r$ along its axis. When two such capsules overlap, we define the points of intersection on each cell ($\mathbf{z}$ in figure 1.2) as follows. First we find the closest points on each cell's axis line segment. The line joining these points then intersects each cell surface at points labelled $\mathbf{z}$, where it is normal to the surface. Hence we have defined contact points on each cell, and the normal to the contact $\hat{\mathbf{n}}$. The distance of overlap d for each contact is then determined by the distance between the contact points along the contact normal direction (figure 1.2).

In order to constrain the system of cells to produce a physically possible, non-overlapping arrangement, we must find the impulse applied to each cell $\Delta\tilde{\mathbf{p}}$ that produces a change in the overlap distance so that $d = 0$ for each contact. We have just described how these overlap distances are changed by a set of applied impulses, and so we can now formulate the constraint system.

1.2.5 Constraint formulation

To form a physically possible arrangement of cells after increasing their length we wish to apply constraint impulses to cells such that

$$\begin{aligned} \mathbf{d} + \Delta\mathbf{d} &= 0 \\ \Delta\mathbf{d} &= -\mathbf{d} \end{aligned}$$

As shown above the change in overlaps $\Delta\mathbf{d}$ produced by a set of generalised impulses $\Delta\tilde{\mathbf{p}}$ means that

$$\mathbf{B}\mathbf{M}^{-1}\Delta\tilde{\mathbf{p}} = \mathbf{A}\Delta\tilde{\mathbf{p}} = \Delta\mathbf{d}$$

where $\mathbf{A}$ is a block matrix $n_{\text{contacts}} \times n_{\text{cells}}$, $\Delta\tilde{\mathbf{p}}$ is a block vector $n_{\text{cells}} \times 1$ and $\mathbf{d}$ is $n_{\text{contacts}} \times 1$. Hence the constrained system is given by:

$$\mathbf{A}\Delta\tilde{\mathbf{p}} + \mathbf{d} = 0$$

Hence we have formulated the system of constraints as a linear system. Given the solution of this system, the change in generalised position of each cell is then $\mathbf{M}^{-1}\Delta\tilde{\mathbf{p}}$. However it is clear that in general this linear system does not have a unique solution. To see this consider that cells may move perpendicular to the normal(s) of their contact(s) without affecting $\Delta\mathbf{d}$.

1.2.6 Energy minimising solution

The least squares solution of the constraint system is:

$$\underset{\Delta\mathbf{p}}{\operatorname{argmin}} \left\{ \|\mathbf{A}\Delta\tilde{\mathbf{p}} + \mathbf{d}\|^2 \right\}$$

where the expression $\mathbf{A}\Delta\tilde{\mathbf{p}} + \mathbf{d}$ is the vector of overlap distances of each contact after application of impulses $\Delta\tilde{\mathbf{p}}$. If we interpret the least-squares solution as an energy minimising solution, where the energy is associated with the overlap of each contact. If the overlap at each contact is ϵ, and if the energy is stored in an elastic fashion, then this energy is:

$$\frac{1}{2}\epsilon^T\mathbf{K}\epsilon = \frac{1}{2}\left\|\sqrt{\mathbf{K}}\epsilon\right\|^2 = \frac{1}{2}\left\|\sqrt{\mathbf{K}}\left(\mathbf{A}\Delta\tilde{\mathbf{p}} + \mathbf{d}\right)\right\|^2$$

where $\mathbf{K}$ is a diagonal stiffness coefficient matrix. So it is implicit in the above minimisation that $\mathbf{K} = 2\mathbf{I}$. If all the stiffnesses are the same (i.e. $\mathbf{K} = K\mathbf{I}$), then this makes no difference to the solution. If some contacts

softer than others are required, the corresponding entry should be changed such that $K_i < 1$. We use this approach to approximate the effect of a soft agarose substrate. This is a bit of distraction for now, so lets just stick with $\mathbf{K} = \mathbf{I}$.

As explained above the matrix $\mathbf{A}$ will typically be poorly conditioned, and the matrix $\mathbf{A}^T\mathbf{A}$ will be even worse. So we still can't get a unique solution. The usual approach is to use regularisation to 'select' a solution. Following the energy minimisation formalism the solution obtained should minimise the work done or energy expended by the constraint impulses. Given an impulse $\Delta\tilde{\mathbf{p}}$ and time step Δt, the average force applied over the time step is $\mathbf{F} = \Delta\tilde{\mathbf{p}}/\Delta t$. The work done by these forces is then

$$\begin{aligned} W &= \mathbf{F}\Delta\tilde{\mathbf{x}} \\ &= \mathbf{F}\mathbf{M}^{-1}\Delta\tilde{\mathbf{p}} \\ &= \frac{1}{\Delta t}\Delta\tilde{\mathbf{p}}^{\mathrm{T}}\mathbf{M}^{-1}\Delta\tilde{\mathbf{p}} \end{aligned}$$

Combining this with the overlap energy described above leads to the problem

$$\underset{\Delta\mathbf{p}}{\operatorname{argmin}} \left\{ \|\mathbf{A}\Delta\tilde{\mathbf{p}} + \mathbf{d}\|^2 + \frac{\alpha}{\Delta t}\Delta\tilde{\mathbf{p}}^{\mathrm{T}}\mathbf{M}^{-1}\Delta\tilde{\mathbf{p}} \right\}$$

where α is a regularisation parameter. In this case we can interpret α physically as the relative energy cost of cell-cell overlap (e.g. due to deformation of the cell wall) compared to the energy cost in overcoming drag. Differentiating the above total energy, and setting to zero gives:

$$\left(\mathbf{A}^{\mathrm{T}}\mathbf{A} + \frac{\alpha}{\Delta t}\mathbf{M}^{-1}\right)\Delta\tilde{\mathbf{p}} = -\mathbf{A}^{\mathrm{T}}\mathbf{d} \tag{1.3}$$

It is now clear that *any* quadratic energy term can be included in the system by forming the appropriate matrix $\mathbf{H}$ such that the energy is given by $E = \|\mathbf{H}\Delta\tilde{\mathbf{p}}\|^2$. Or maybe more usefully, the energy can be defined directly in terms of change in generalised position $\Delta\tilde{\mathbf{x}}$ as $E = \|\mathbf{G}\Delta\tilde{\mathbf{x}}\|^2 = \|\mathbf{G}\mathbf{M}^{-1}\Delta\tilde{\mathbf{p}}\|^2$, and the linear system is then given by

$$\left(\frac{1}{\alpha}\mathbf{A}^{\mathrm{T}}\mathbf{A} + \frac{1}{\Delta t}\mathbf{M}^{-1} + \mathbf{M}^{-1}\mathbf{G}^{\mathrm{T}}\mathbf{G}\mathbf{M}^{-1}\right)\Delta\tilde{\mathbf{p}} = -\mathbf{A}^{\mathrm{T}}\mathbf{d} \tag{1.4}$$

where I have moved the α to make clear its physical interpretation as the relative cost of overlap. Note also I have used the fact that $\mathbf{M}^{-\mathrm{T}} \equiv \mathbf{M}^{-1}$ because it is diagonal except for terms involving the projection matrices $\mathbf{P}_i$, which are themselves symmetric by definition.

Note. *Writing out the matrix $\mathbf{A} = \mathbf{B}\mathbf{M}^{-1}$ and $\Delta\tilde{\mathbf{p}} = \mathbf{M}\Delta\tilde{\mathbf{x}}$ in the above system gives a factor of $\mathbf{M}^{-1}$ which could be eliminated. However, this is actually acting as a right-preconditioner. Similarly expanding $\mathbf{A}^T = \mathbf{M}^{-1}\mathbf{B}^T$ gives us left-preconditioning. Hence we have split-preconditioning. I'm pretty sure we did some testing and the preconditioning did improve the condition number.*

Note. *The factor of $1/\Delta t$ is not computed in the current code. At the time we were considering a kind of ad hoc regularisation term rather than explicitly minimising physical work. Adding the $1/\Delta t$ makes sense.*

Note. *In the current code the viscosity from substrate per unit length of cells μ is set at $\mu = 1$ - i.e. it is factored out of the $\mathbf{M}^{-1}$ matrices. This means that the parameter α incorporates the value of μ into the ratio of drag from the substrate to resistance to deformation of cells. It seems sensible that this should be the same as the ratio $\Gamma = \mu/\gamma$, where γ is the resistance to change in length (see appendix). This would be nice because the whole model would then be parameterised only by Γ. Need to think about this a bit more.*

1.3 Adhesion

Now we want to form a matrix $\mathbf{G}$ that adds a quadratic energy to the system to simulate adhesion. Consider adhesion that acts only in the plane of the cell surface at each contact (tangent plane), such that $E_k =$

$(\Delta d_k^\perp)^2 = \|\Delta \mathbf{d}_k^\perp\|^2$ where $\Delta \mathbf{d}_k^\perp$ is the movement vector in the tangent plane between contact points on each cell involved in contact k. This is a 3×1 vector that is the projection of the total movement into the tangent plane of the contact. In this case

$$\mathbf{G}\mathbf{M}^{-1}\Delta\tilde{\mathbf{p}} = \Delta \mathbf{d}^\perp$$

where the matrices and vectors are in block form, with one block per cell or contact.

This matrix $\mathbf{G}$ is closely related to the above described $\mathbf{B}$ matrix, which projects the movement of each contact point along its respective contact normal $\hat{\mathbf{n}}_k$. The tangent plane is perpendicular to this normal vector. For cell i and contact k,

$$\mathbf{B}_{ik} = \begin{bmatrix} \hat{\mathbf{n}}_k^{\mathrm{T}} & -\left(\hat{\mathbf{n}}_k \times \mathbf{z}_{ik}\right)^{\mathrm{T}} & \frac{(\hat{\mathbf{n}}_k \cdot \hat{\mathbf{a}}_i)(\mathbf{z}_{ik} \cdot \hat{\mathbf{a}}_i)}{l_0} \end{bmatrix}$$

where $\mathbf{B}_{ik}$ is a 1×7 matrix. The matrix blocks $\mathbf{G}_{ik}$ are 3×7 and given by

$$\begin{aligned} \mathbf{G}_{ik} &= \begin{bmatrix} \mathbf{Q} & \mathbf{Q}\mathbf{Z}_{ik}^{\times} & \left[\hat{\mathbf{a}}_i - \hat{\mathbf{n}}_k \left(\hat{\mathbf{n}}_k \cdot \hat{\mathbf{a}}_i\right)\right] \frac{(\mathbf{z}_{ik} \cdot \hat{\mathbf{a}}_i)}{l_0} \end{bmatrix} \\ &= \begin{bmatrix} \mathbf{Q} & \mathbf{Q}\mathbf{Z}_{ik}^{\times} & \frac{(\mathbf{z}_{ik} \cdot \hat{\mathbf{a}}_i)}{l_0} \mathbf{Q}\hat{\mathbf{a}}_i \end{bmatrix} \\ &= \mathbf{Q} \begin{bmatrix} \mathbf{I} & \mathbf{Z}_{ik}^{\times} & \frac{(\mathbf{z}_{ik} \cdot \hat{\mathbf{a}}_i)}{l_0} \hat{\mathbf{a}}_i \end{bmatrix} \end{aligned}$$

Here $\mathbf{Q}$ is the 3×3 matrix projecting into the tangent plane, so that for any vector $\mathbf{u}$

$$\mathbf{Q}\mathbf{u} = \mathbf{u} - \hat{\mathbf{n}}_k \left(\hat{\mathbf{n}}_k \cdot \mathbf{u}\right) \tag{1.5}$$

and $\mathbf{Z}_{ik}^{\times}$ is the matrix representing the cross product

$$\mathbf{Z}_{ik}^{\times}\mathbf{u} = \mathbf{z}_{ik} \times \mathbf{u} \tag{1.6}$$

These first two blocks ($\mathbf{Q}$ and $\mathbf{Q}\mathbf{Z}_{ik}^{\times}$) of $\mathbf{G}_{ik}$ are 3×3 and the third ($\frac{(\mathbf{z}_{ik} \cdot \hat{\mathbf{a}}_i)}{l_0}\mathbf{Q}\mathbf{a}_i$) is 3×1.

Note. *We could explicitly store the 3×3 blocks and apply them as matrix multiplications. However, it is more efficient to do the computation directly using equations 1.5 and 1.6.*

Note. *The result of applying each block $\mathbf{G}_{ik}$ to the cells impulse $\Delta\tilde{\mathbf{p}}_i$ is a 3×1 vector. Hence the array storing the result of $\mathbf{G}\Delta\tilde{\mathbf{p}}$ must use `float4` types. This might seem counterintuitive since the distances are projected onto a plane, but note that the tangent plane of each contact is in general different.*

1.4 Viscous adhesion

Because we recompute the closest points for contacts at each time step the above described adhesion energy will be completely dissipated. This is effectively a viscous model in which

$$\mathbf{F} = C\frac{d\mathbf{x}}{dt} \approx C\frac{\Delta\mathbf{x}}{\Delta t}$$

and thus $E \approx \frac{1}{\Delta t} C\|\Delta\mathbf{x}\|^2$. So that using the above analyis the energy from viscous adhesion is given by

$$E = \left(\frac{1}{\Delta t} C\right) \|\mathbf{G}\mathbf{M}^{-1}\Delta\tilde{\mathbf{p}}\|^2$$

for the same viscosity coefficient at each contact. More generally,

$$E = \left(\frac{1}{\Delta t}\right) \Delta\tilde{\mathbf{p}}^{\mathrm{T}}\mathbf{M}^{-1}\mathbf{G}^{\mathrm{T}}\mathbf{C}\mathbf{G}\mathbf{M}^{-1}\Delta\tilde{\mathbf{p}}$$

where $\mathbf{C}$ is a diagonal matrix of viscosity coefficients for each contact. In practice this matrix is best implemented by just scaling each block $\mathbf{G}_{ik}$ by the appropriate coefficient.

Note. *The scaling by $1/\Delta t$ is required to make this purely viscous model physically sensible. To implement a purely elastic model of contact would require keeping track of the original point of contact between each pair of cells.*

1.5 Implementation in CellModeller4

The following table describes which functions or OpenCL kernels perform which calculations and data arrays that contain the results, using the mathematical notation above.

Function/kernel	Maths	Description
`find_contacts`	$\mathbf{d}$, $\hat{\mathbf{n}}$	Finds overlapping cells and computes the overlap distance d_k and surface normal $\hat{\mathbf{n}}_k$ for each contact k.
`rel_dists`	$\mathbf{d}$	Stores the vector of overlap distances, one element (`float`) per contact.
`compute_Minvx`	$\mathbf{M}^{-1}$	Applies the inverse drag matrix to some given vector of length n_{cells} and type `float8` (only first 7 elements are used). It does this per cell, by applying its $\mathbf{M}_i^{-1}$ matrix block.

Appendices

Appendix A

Equations of motion

Consider a capsule with main axis $\hat{\mathbf{a}}$, mass m, and length l. When in motion the capsule is associated with linear ($\mathbf{v}_{\text{lin}}$), angular ($\mathbf{w}$), and growth (v_{growth}) velocities (figure 1.1b). Now consider a point on the surface of the capsule with position $\mathbf{r}$ relative to the capsule's center of mass. The velocity of that point is given by:

$$\begin{aligned}\mathbf{v}_r &= \mathbf{v}_{\text{lin}} + \mathbf{w} \times \mathbf{r} + \frac{1}{2}\frac{\hat{\mathbf{a}} \cdot \mathbf{r}}{l_0}\hat{\mathbf{a}} v_{\text{growth}} \\ &= \mathbf{v}_{\text{lin}} - \mathbf{r} \times \mathbf{w} + \frac{1}{2}\frac{\hat{\mathbf{a}} \cdot \mathbf{r}}{l_0}\hat{\mathbf{a}} v_{\text{growth}}\end{aligned}$$

where l_0 is the current capsule length. The first term in this expression is the linear velocity of the whole cell, the second term is the angular component, and the final term is due to growth. Growth is assumed to occur by extension of all parts of the cell wall along the axis, meaning that any point on the cell is moving away from the centre of mass at a rate proportional to its distance from the centre. The maximum velocity due to growth then occurs at the tips of the cell which are each moving away from the centre of mass at rate $\frac{1}{2}v_{\text{growth}}$ along the cell axis $\hat{\mathbf{a}}$.

Each point on the cell surface experiences viscous drag from the growth substrate due to its motion. The viscous drag force on a differential length dr of the capsule is approximately given by:

$$d\mathbf{F} = -\mu dr \mathbf{v}_r$$

where μ is a drag coefficient per unit length. To understand the motion of the capsule shape, initially at rest, after the application of a generalised impulse $\Delta\tilde{\mathbf{p}}$, which can be divided into linear, angular and growth components $\begin{pmatrix} \Delta\mathbf{p} & \Delta\mathbf{L} & \Delta g \end{pmatrix}^T$, we must find the net force on the capsule due to viscous drag at each point on its surface. Given this force, Newton's laws can be applied to find the change in generalised position.

A.1 Linear impulse $\Delta\mathbf{p}$

Approximating the forces on the differential length element at the average position, so that position $\mathbf{r} = r\hat{\mathbf{a}}$ lies on the axis of the cell:

$$\begin{aligned}d\mathbf{F} &= -\mu dr \mathbf{v}_r \\ d\mathbf{F} &= -\mu dr \left(\mathbf{v}_{\text{lin}} - \mathbf{r} \times \mathbf{w} + \frac{1}{2}\frac{\hat{\mathbf{a}} \cdot \mathbf{r}}{l_0}\hat{\mathbf{a}} v_{\text{growth}}\right) \\ d\mathbf{F} &= -\mu dr \left(\mathbf{v}_{\text{lin}} - r\hat{\mathbf{a}} \times \mathbf{w} + \frac{1}{2}\frac{r}{l_0}\hat{\mathbf{a}} v_{\text{growth}}\right)\end{aligned}$$

The total force on the capsule is given by the integral over the length of the capsule from $-\frac{l_0}{2}$ to $+\frac{l_0}{2}$. The second two terms in the expression for velocity are odd in r and so will cancel when integrated so the total force on the capsule is:

$$\begin{aligned}\mathbf{F} &= -\mu \mathbf{v}_{\text{lin}} \int_{-\frac{l_0}{2}}^{+\frac{l_0}{2}} dr \\ &= -\mu \mathbf{v}_{\text{lin}} l_0\end{aligned}$$

And following Newton's laws:

$$\begin{aligned}m\frac{d\mathbf{v}_{\text{lin}}}{dt} &= -\mu l_0 \mathbf{v}_{\text{lin}} \\ \mathbf{v}_{\text{lin}} &= v_0 \exp\left(-\frac{\mu l_0}{m} t\right) \\ &= \frac{\Delta \mathbf{p}}{m} \exp\left(-\frac{\mu l_0}{m} t\right)\end{aligned}$$

The change in position of the centre of mass of the capsule $\mathbf{x}$ due to linear impulse $\Delta\mathbf{p}$, and thus the change in position of any point on the cell is then found as:

$$\begin{aligned}\frac{d\mathbf{x}}{dt} &= \frac{\Delta \mathbf{p}}{m} \exp\left(-\frac{\mu l_0}{m} t\right) \\ \Delta \mathbf{x} &= \frac{\Delta \mathbf{p}}{\mu l_0} \left(1 - \exp\left(-\frac{\mu l_0}{m} t\right)\right)\end{aligned}$$

In the case of a bacterium, inertial effects are very small compared to drag forces [**?**] meaning $m/\mu \approx 0$, so that the exponential term is nearly zero and so:

$$\Delta \mathbf{x} \approx \frac{\Delta \mathbf{p}}{\mu l_0} \tag{A.1}$$

A.2 Angular impulse ΔL

Now consider the rotational motion of the cell. The torque applied at a differential section of the cell at position $\mathbf{r} = r\hat{\mathbf{a}}$ is:

$$\begin{aligned}d\tau &= \mathbf{r} \times d\mathbf{F} \\ &= \mathbf{r} \times -\mu dr \mathbf{v}_r \\ &= \mathbf{r} \times -\mu dr \left(\mathbf{v}_{\text{linear}} - r\hat{\mathbf{a}} \times \mathbf{w} + \frac{1}{2}\frac{r}{l_0}\hat{\mathbf{a}} v_{\text{growth}}\right)\end{aligned}$$

The drag force due to linear velocity makes no total contribution to torque (the contributions on the two sides of the capsule's center of mass cancel) and neither does drag force due to growth velocity (it is parallel to $\mathbf{r}$). Note that the triple product:

$$\begin{aligned}\mathbf{r} \times (\mathbf{w} \times \mathbf{r}) &= \mathbf{w}(\mathbf{r} \cdot \mathbf{r}) - \mathbf{r}(\mathbf{r} \cdot \mathbf{w}) \\ &= \mathbf{w} r^2 - \mathbf{r}(\mathbf{r} \cdot \mathbf{w})\end{aligned}$$

and so:

$$\begin{aligned} d\tau &= -\mu \left(\mathbf{w} r^2 - r\hat{\mathbf{a}}(r\hat{\mathbf{a}} \cdot \mathbf{w}) \right) dr \\ &= -\mu \left(\mathbf{w} - \hat{\mathbf{a}}(\hat{\mathbf{a}} \cdot \mathbf{w}) \right) r^2 dr \\ \tau &= -\mu \left(\mathbf{w} - \hat{\mathbf{a}}(\hat{\mathbf{a}} \cdot \mathbf{w}) \right) \int_{-\frac{l_0}{2}}^{\frac{l_0}{2}} r^2 dr \\ &= -\frac{1}{12} \mu l_0^3 \left(\mathbf{w} - \hat{\mathbf{a}}(\hat{\mathbf{a}} \cdot \mathbf{w}) \right) = \mathbf{I} \frac{d\mathbf{w}}{dt} \end{aligned}$$

The expression $\mathbf{w} - \hat{\mathbf{a}}(\hat{\mathbf{a}} \cdot \mathbf{w})$ represents a projection of the vector $\mathbf{w}$ onto the plane perpendicular to the axis $\hat{\mathbf{a}}$, and can be written as $\mathbf{P}\mathbf{w}$ where $\mathbf{P}$ is the appropriate projection matrix:

$$\begin{aligned} \tau &= -\frac{1}{12} \mu l_0^3 \mathbf{P}\mathbf{w} = I \frac{d\mathbf{w}}{dt} \\ \mathbf{w} &= \mathbf{w}_0 \exp\left(-\frac{\mu l_0^3 \mathbf{P} t}{12 I} \right) \end{aligned}$$

For a projection matrix $\mathbf{P}$, an exponential of the form $\exp(k\mathbf{P})$, where k is a scalar, is:

$$\exp(k\mathbf{P}) = \mathbf{P} \exp(k) + (\mathbf{I} - \mathbf{P})$$

so:

$$\mathbf{w} = \mathbf{P}\mathbf{w}_0 \exp\left(-\frac{\mu l_0^3 t}{12 I} \right) + (\mathbf{I} - \mathbf{P}) \mathbf{w}_0$$

In which the second term $(\mathbf{I} - \mathbf{P}) \mathbf{w}_0$ is the angular velocity about the cell axis $\hat{\mathbf{a}}$. Approximating the capsule as a 'slender rod' with no rotational inertia about its axis the second term can be ignored, and:

$$\begin{aligned} \mathbf{w} &= \mathbf{P}\mathbf{w}_0 \exp(-\frac{\mu l_0^3}{12 I} t) \\ &= \frac{\mathbf{P}\Delta\mathbf{L}}{I} \exp(-\frac{\mu l_0^3}{12 I} t) = \frac{d\theta}{dt} \end{aligned}$$

Making the same approximation for negligible inertia as above $I/\mu \approx 0$ gives:

$$\Delta\theta \approx \frac{12 \mathbf{P}\Delta\mathbf{L}}{\mu l_0^3} \tag{A.2}$$

So, the effect of a rotational impulse is projected onto the plane of the cell axis - that is, it only causes rotation about the other two axes.

A.3 Growth impulse Δg

A growth impulse tends to elongate the cell, and is resisted by compressive forces along the axis of the capsule due to drag:

$$
\begin{aligned}
F_c &= \mu \frac{1}{2} \left[\int_0^{\frac{l_0}{2}} \frac{r}{l_0} v_{\text{growth}} dr - \int_{-\frac{l_0}{2}}^{0} \frac{r}{l_0} v_{\text{growth}} dr \right] \\
&= \frac{\mu}{2} v_{\text{growth}} \left[\int_0^{\frac{l_0}{2}} \frac{r}{l_0} dr - \int_{-\frac{l_0}{2}}^{0} \frac{r}{l_0} dr \right] \\
&= \frac{\mu l_0}{8} v_{\text{growth}}
\end{aligned}
$$

This is the drag due to interaction with the substrate. In order to model the cell's resistance to change in length due to its own structural and mechanical properties, I incorporate an additional drag term:

$$
F_c = \left(\frac{\mu l_0}{8} + \gamma \right) v_{\text{growth}}
$$

where γ describes cell growth drag. Following the same reasoning as above, integrating and neglecting inertial effects, and assuming that $\Delta l << l$ so that l_0 can be taken as constant, the effect of growth impulse δg on cell length is:

$$
\Delta l \approx \frac{8 \Delta g}{\mu l_0 + 8\gamma}
$$

where Δg is the applied growth impulse. Assuming that the resistance of the cell to deformation dominates viscous drag from the substrate, then this can be reduced to:

$$
\Delta l \approx \frac{\Delta g}{\gamma} \tag{A.3}
$$

A.4 Motion due to generalised impulse

Combining the results for each component of motion from equations A.1, A.2 and A.3, the change in generalised position $\tilde{\mathbf{x}} = \begin{pmatrix} \mathbf{x} & \theta & l \end{pmatrix}^T$ after the application of a general impulse $\Delta\tilde{\mathbf{p}} = \begin{pmatrix} \Delta\mathbf{p} & \Delta\mathbf{L} & \Delta g \end{pmatrix}^T$ can be written in block matrix form as:

$$
\Delta\tilde{\mathbf{x}} = \begin{bmatrix} \frac{\Delta\mathbf{p}}{\mu l_0} \\ \frac{12\mathbf{P}\Delta\mathbf{L}}{\mu l_0^3} \\ \frac{\Delta g}{\gamma} \end{bmatrix} \tag{A.4}
$$

$$
= \begin{bmatrix} \text{diag}(\frac{1}{\mu l_0}) & 0 & 0 \\ 0 & \frac{12\mathbf{P}}{\mu l_0^3} & 0 \\ 0 & 0 & \frac{1}{\gamma} \end{bmatrix} \begin{bmatrix} \Delta\mathbf{p} \\ \Delta\mathbf{L} \\ \Delta g \end{bmatrix} \tag{A.5}
$$