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MODELLING CELL MOTILITY AND CHEMOTAXIS WITH EVOLVING SURFACE FINITE ELEMENTS: SUPPLEMENTARY MATERIAL

CHARLES M. ELLIOTT, BJÖRN STINNER, AND CHANDRASEKHAR VENKATARAMAN

1. NOTATION AND PRELIMINARIES

Here we define our notation and some basic facts and identities from differential geometry. For further details and proofs of the results we state we refer to the book by Do Carmo [1]. Throughout Γ denotes a closed smooth oriented $d - 1$ dimensional hypersurface in \mathbb{R}^d , $d = 2, 3$, with *outward* pointing unit normal $\boldsymbol{\nu}$. For $\boldsymbol{x} \in \Gamma$ we will make the slight abuse of notation and denote by \boldsymbol{x} both the point \boldsymbol{x} in Γ and the identity map $I_\Gamma : \Gamma \rightarrow \Gamma : I_\Gamma(\boldsymbol{x}) = \boldsymbol{x}$. Given a function η defined in a neighbourhood of Γ , the tangential or surface gradient of η denoted by ∇_Γ is defined as

$$(1.1) \quad \nabla_\Gamma \eta := \nabla \eta - \nabla \eta \cdot \boldsymbol{\nu} \boldsymbol{\nu},$$

where ∇ denotes the Cartesian gradient in \mathbb{R}^d . The Laplace-Beltrami operator Δ_Γ is defined as the tangential divergence of the tangential gradient, i.e.,

$$(1.2) \quad \Delta_\Gamma \eta := \nabla_\Gamma \cdot (\nabla_\Gamma \eta).$$

The mean curvature H of Γ with respect to the normal $\boldsymbol{\nu}$ is defined as

$$(1.3) \quad H := \nabla_\Gamma \cdot \boldsymbol{\nu}.$$

Note that by this definition the mean curvature is the sum of the principal curvatures and differs from the more common definition by a factor $\frac{1}{d-1}$. Note also that our sign convention is such that the unit sphere has *positive* mean curvature if $\boldsymbol{\nu}$ is the unit outer normal. A fundamental identity that underpins the numerical method is the following relationship between the Laplace-Beltrami of the identity map and the mean curvature vector

$$(1.4) \quad \Delta_\Gamma \boldsymbol{x} = -H \boldsymbol{\nu}.$$

Another identity we shall make use of when approximating higher order geometric flows on surfaces is for a smooth vector valued function $\boldsymbol{\eta}$

$$(1.5) \quad \int_\Gamma \nabla_\Gamma \cdot \boldsymbol{\eta} = \int_\Gamma H \boldsymbol{\eta} \cdot \boldsymbol{\nu}.$$

Here and throughout, for $\boldsymbol{f} \in \mathbb{R}^d$, $\nabla_\Gamma \boldsymbol{f} \in \mathbb{R}^{d \times d}$ is such that $(\nabla_\Gamma \boldsymbol{f})_{ij} = [\nabla_\Gamma f_i]_j$, $i, j = 1, \dots, d$. Applying the above identity with $\boldsymbol{\eta} = \Phi \boldsymbol{\nu}$, where $\Phi \in H^1(\Gamma(t))^{d \times d}$ is an arbitrary test function, gives

$$(1.6) \quad \int_\Gamma \nabla_\Gamma \boldsymbol{\nu} \cdot \Phi = - \int_\Gamma \boldsymbol{\nu} \cdot (\nabla_\Gamma \cdot \Phi) + \int_\Gamma H \boldsymbol{\nu} \cdot \Phi \boldsymbol{\nu}.$$

Here and throughout, for $\Phi \in \mathbb{R}^{d \times d}$, $\nabla_\Gamma \cdot \Phi \in \mathbb{R}^d$ is such that $[\nabla_\Gamma \cdot \Phi]_i = \nabla_\Gamma \cdot \Phi_i$, $i = 1, \dots, d$. The expression (1.6) is employed in our approximation of the Weingarten map on discrete evolving surfaces.

2. VARIATIONAL FORMULATION

Here we discuss the variational formulation of the surface evolution law and the corresponding finite element discretisation. We start with the following remark which we employ in our approximations of cell motility in 2d:

2.1. Remark (Weingarten map on a closed curve). For the case $d = 2$, i.e., Γ a closed curve, we have that $|\nabla_\Gamma \boldsymbol{\nu}|^2 = H^2$. Thus the surface evolution law and the corresponding numerical schemes simplify considerably as we do not have to directly compute an approximation of the Weingarten map.

The discretisation with surface finite elements requires an appropriate variational formulation of both the membrane evolution equation but also the surface reaction-diffusion system (RDS). For the latter one we propose to proceed as in [2]: For $i = 1, \dots, m$, find $a_i \in H^1(\Gamma(t))$ such that

$$(2.1) \quad \frac{d}{dt} \int_{\Gamma(t)} a_i \chi + \int_{\Gamma(t)} D_i \nabla_{\Gamma(t)} a_i \cdot \nabla_{\Gamma(t)} \chi = \int_{\Gamma(t)} a_i \partial^\bullet \chi + \int_{\Gamma(t)} f_i(\mathbf{a}) \chi \quad \forall \chi \in H^1(\Gamma(t))$$

The variational formulation of the membrane equation couples to a variational formulation of the identity (1.4) which will serve to compute the mean curvature on the evolving polyhedral surface or curve and a variational formulation based on the identity (1.6) for the computation of the Weingarten map on an evolving polyhedral surface (c.f. Remark 2.1): Find $\mathbf{x} \in H^1(\Gamma(t))^3$ and $H \in H^1(\Gamma(t))$ such that

$$(2.2) \quad \begin{aligned} \int_{\Gamma(t)} \nabla_{\Gamma(t)} \boldsymbol{\nu} \cdot \Phi &= - \int_{\Gamma(t)} \boldsymbol{\nu} \cdot \nabla_{\Gamma(t)} \cdot \Phi + \int_{\Gamma(t)} (H \boldsymbol{\nu}) \cdot (\Phi \boldsymbol{\nu}) \\ \int_{\Gamma(t)} \left(\partial_t \mathbf{x} \cdot \boldsymbol{\nu} \chi + k_b \nabla_{\Gamma(t)} H \cdot \nabla_{\Gamma(t)} \chi - k_b H |\nabla_\Gamma \boldsymbol{\nu}|^2 \chi + \frac{1}{2} k_b H^3 \chi + k_s H \right) \\ &= \int_{\Gamma(t)} (\lambda \chi + \mathbf{k}_p \cdot \mathbf{a} \chi + \mathcal{F}_{ext} \chi) \\ \int_{\Gamma(t)} (H \boldsymbol{\nu} \cdot \boldsymbol{\chi} - \nabla_{\Gamma(t)} \mathbf{x} : \nabla_{\Gamma(t)} \boldsymbol{\chi}) &= 0, \end{aligned}$$

for all $\chi \in H^1(\Gamma(t))$, $\boldsymbol{\chi} \in H^1(\Gamma(t))^3$, $\Phi \in H^1(\Gamma(t))^{3 \times 3}$. Here for simplicity we have assumed the viscous surface evolution law (c.f. main text) is nondimensionalised such that $\omega = 1$.

3. NUMERICAL METHOD

For the interested reader we provide a detailed technical description of the numerical methods we employ. Discretising the time interval $[0, T]$ into a partition of N (possibly variable) subintervals, $0 < t_1 \dots < t_N = T$, we denote by $\tau_m := t_m - t_{m-1}$, $m \in (1, \dots, N)$ the timestep. The method we employ is based on parameterising the surface $\Gamma_h^{m+1} := \Gamma_h(t_{m+1})$ over Γ_h^m . We define the following surface finite element spaces:

3.1. Definition (Piecewise linear surface finite element space). Given a triangulated surface Γ_h we define the following space of piecewise linear C^0 functions

$$(3.1) \quad \mathbb{V}(\Gamma_h) := \{\chi \in C(\Gamma_h) : \chi|_s \text{ is linear } \forall s \in \mathcal{T}_h\}.$$

Given a triangulated surface $\tilde{\Gamma}_h$, a quadratic triangulated surface Γ_h is defined as

$$(3.2) \quad \Gamma_h = \cup_{s \in \mathcal{T}_h} s,$$

where there exists a homeomorphism $\mathcal{G} : \tilde{\Gamma}_h \rightarrow \Gamma_h$ such that

- for each $s \in \mathcal{T}_h$ there is a $\tilde{s} \in \tilde{\mathcal{T}}_h$ with $s = \mathcal{G}(\tilde{s})$,
- \mathcal{G} is a polynomial of degree 2 on each $\tilde{s} \in \tilde{\mathcal{T}}_h$,
- \mathcal{G} leaves vertices unchanged.

3.2. Definition (Isoparametric quadratic surface finite element space). Given a quadratic triangulated surface Γ_h we define the following space of piecewise linear C^0 functions

$$(3.3) \quad \mathbb{V}_2(\Gamma_h) := \{\chi \in C(\Gamma_h) : \chi|_s \text{ is quadratic } \forall s \in \mathcal{T}_h\}.$$

We will also make use of the discrete surface normal defined as $\nu_h^n := \frac{(\mathbf{X}_h^n)^\perp}{|\mathbf{X}_h^n|}$ for curves and the normalised weighted (by element area) sum of the normals over the patch of elements shared by a single vertex for surfaces [3].

3.3. Problem (Discrete curve evolution). Our method to approximate the solution to (2.2), for the case of Γ a closed curve (c.f., Remark 2.1), is: for $n = 0, \dots, N-1$, given $\mathbf{X}_h^n \in (\mathbb{V}^n)^2$, $H_h^n \in \mathbb{V}^n$ and $\mathbf{a}_h^n \in (\mathbb{V}^n)^m$, find $\mathbf{X}_h^{n+1} \in (\mathbb{V}^n)^2$, $H_h^{n+1} \in \mathbb{V}^n$ such that

$$(3.4) \quad \begin{aligned} \int_{\Gamma_h^n} \left(\frac{1}{\tau_{n+1}} (\mathbf{X}_h^{n+1} - \mathbf{X}_h^n) \nu_h^n \chi_h + k_b \nabla_{\Gamma_h^n} H_h^{n+1} \cdot \nabla_{\Gamma_h^n} \chi_h - \frac{1}{2} k_b (H_h^n)^2 H_h^{n+1} \chi_h + k_s H_h^{n+1} \chi_h \right) \\ = \int_{\Gamma_h^n} \left(\lambda^{n+1} + \mathbf{k}_p \cdot \mathbf{a}_h^m + \mathcal{F}_{ext}^n \cdot \nu_h^n \right) \chi_h \\ \int_{\Gamma_h^n} (H_h^{n+1} \nu_h^n \cdot \chi_h - \nabla_{\Gamma_h^n} \mathbf{X}_h^{n+1} : \nabla_{\Gamma_h^n} \chi_h) = 0, \end{aligned}$$

for all $\chi_h \in \mathbb{V}^n$, $\chi_h \in (\mathbb{V}^n)^2$.

3.4. Problem (Discrete surface evolution). Our method to approximate the solution to (2.2), for the case of Γ a closed surface, is: for $n = 0, \dots, N-1$, given $\mathbf{X}_h^n \in (\mathbb{V}_2^n)^3$, $H_h^n \in \mathbb{V}_2^n$ and $\mathbf{a}_h^n \in (\mathbb{V}_2^n)^m$, first find $\mathbf{Q}_h^n \in (\mathbb{V}_2^n)^{3 \times 3}$ such that

$$(3.5) \quad \int_{\Gamma_h^n} \mathbf{Q}_h^n \Phi_h = \int_{\Gamma_h^n} (H_h^n \nu_h^n \Phi_h \nu_h^n - \nu_h^n \nabla_{\Gamma_h^n} \cdot \Phi_h) \quad \forall \Phi_h \in (\mathbb{V}_2^n)^{3 \times 3},$$

then find $\mathbf{X}_h^{n+1} \in (\mathbb{V}_2^n)^3$, $H_h^{n+1} \in \mathbb{V}_2^n$ such that

$$(3.6) \quad \begin{aligned} \int_{\Gamma_h^n} \left(\frac{1}{\tau_{n+1}} (\mathbf{X}_h^{n+1} - \mathbf{X}_h^n) \nu_h^n \chi_h + k_b \nabla_{\Gamma_h^n} H_h^{n+1} \cdot \nabla_{\Gamma_h^n} \chi_h - k_b |\mathbf{Q}_h^n|^2 H_h^{n+1} \chi_h + k_s H_h^{n+1} \chi_h \right) \\ = \int_{\Gamma_h^n} \left(-\frac{k_b}{2} (H_h^n)^3 \chi_h + \lambda^{n+1} \chi_h + \mathbf{k}_p \cdot \mathbf{a}_h^m \chi_h + \mathcal{F}_{ext}^n \cdot \nu_h^n \chi_h \right) \\ \int_{\Gamma_h^n} (H_h^{n+1} \nu_h^n \cdot \chi_h - \nabla_{\Gamma_h^n} \mathbf{X}_h^{n+1} : \nabla_{\Gamma_h^n} \chi_h) = 0, \end{aligned}$$

for all $\chi_h \in \mathbb{V}_2^n$, $\chi_h \in (\mathbb{V}_2^n)^3$.

We use a Newton method which is described in detail by Bonito et al. [4] and Elliott and Stinner [5] to determine the Lagrange multiplier λ^{n+1} such that the volume enclosed by the surface is conserved to a desired tolerance.

We use the identity (1.4) to compute an initial value for the mean curvature $H_h^0 \in \mathbb{V}^0$ as the solution of

$$(3.7) \quad \int_{\Gamma_h^0} H_h \nu_h^0 \chi_h = \int_{\Gamma_h^0} \nabla_{\Gamma_h} \mathbf{X}_h^0 \chi_h,$$

for all $\chi_h \in (\mathbb{V}^n)^d$.

When modelling cell movement in three-dimensions we use spatial adaptivity, specifically h -refinement, to reduce the computational cost of the method. Our adaptive strategy seeks to refine (bisect) elements

of the triangulation in regions with large curvature or if the mesh-size exceeds a certain tolerance. The strategy which is based on the adaptive strategy employed by Elliott and Stinner [5] is to mark an element for refinement if either

$$(3.8) \quad h_i > \frac{N_H}{I_H} \quad \text{or} \quad h > N_h,$$

where h_i denotes the element mesh-size (maximum edge length), I_h is the mean of the discrete approximation $|Q_h^n|^2$ to the shape operator on the element (an approximation to the sum of squares of the principal curvatures), N_H and N_h are user defined parameters. We mark elements for coarsening (the inverse of refinement) according to the following

$$(3.9) \quad h_i < \frac{M_H}{I_H} \quad \text{and} \quad h < M_h,$$

where $M_H < N_H$ and $M_h < N_h$ are user defined parameters. For more details on mesh adaption, coarsening, refinement and bisection we refer to [6].

The proposed schemes for the approximation of the surface evolution law induce a tangential velocity to the discrete surface evolution, while the material velocity of the continuous surface is geometric (i.e., has zero tangential component). Defining the tangential component of the discrete surface velocity

$$(3.10) \quad \mathbf{T}_h^n := \frac{1}{\tau_n} (\mathbf{X}_h^n - \mathbf{X}_h^{n-1}) - \frac{1}{\tau_n} (\mathbf{X}_h^n - \mathbf{X}_h^{n-1}) \cdot \boldsymbol{\nu}_h^n \boldsymbol{\nu}_h^n,$$

we arrive at the following discrete problem for the surface RDS update which accounts for the induced tangential velocity and is based on the evolving surface finite element method [2].

3.5. Problem (Discrete RDS approximation). Our method to approximate the solution to (2.1) is: for $n = 0, \dots, N-1$, given the discrete surfaces $\Gamma_h^n, \Gamma_h^{n+1}$, the tangential velocity of the parameterisation \mathbf{T}_h^n and $\mathbf{a}_h^n \in (\mathbb{V}^n, \text{ or } \mathbb{V}_2^n)^m$, for $i = 1, \dots, m$ find $(a_h^{n+1})_i \in \mathbb{V}^{n+1}$, or \mathbb{V}_2^{n+1} for $d = 2, 3$ respectively such that

$$(3.11) \quad \int_{\Gamma_h^{n+1}} \left(\frac{1}{\tau_{n+1}} (a_h^{n+1})_i \chi_h^{n+1} - \nabla_{\Gamma_h^{n+1}} \cdot ((a_h^{n+1})_i \mathbf{T}_h^n) \chi_h^{n+1} + D_i \nabla_{\Gamma_h^{n+1}} (a_h^{n+1})_i \nabla_{\Gamma_h^{n+1}} \chi_h^{n+1} \right) \\ = \int_{\Gamma_h^n} \left(\frac{1}{\tau_{n+1}} (a_h^n)_i \chi_h^n + f_i(\mathbf{a}_h^n) \chi_h^n \right),$$

for all $\chi_h^{n+1} \in \mathbb{V}^{n+1}$ or \mathbb{V}_2^{n+1} and all $\chi_h^n \in \mathbb{V}^n$ or \mathbb{V}_2^n for $d = 2, 3$ respectively.

3.6. Modelling noisy signalling due to heterogeneities in the media and the presence of a chemoattractant. When modelling chemotaxis, we assume that receptors on the cells surface sense concentrations of a chemoattractant. This signal is inherently noisy due to the heterogeneous nature of the media in which cells migrate. We model this noisy signalling with an Ornstein-Uhlenbeck process [7] of the following form

$$(3.12) \quad dX^t = \theta(\mu - X^t) dt + \sigma dW^t,$$

where W^t denotes the Wiener process and θ, μ, σ are the rate of reversion to the mean, the mean and the variance respectively.

3.7. The Euler-Maruyama method for the approximation of Ornstein-Uhlenbeck processes. We approximate (3.12) by assuming the signal is constant in each finite element and use an Euler-Maruyama method [8] to approximate the SDE in each element. The method is as follows, for all $s \in \mathcal{T}_h$, given an initial value Y_s^0 , find $Y_s^n, n = 1, \dots, N$ such that

$$(3.13) \quad Y_s^{n+1} = Y_s^n + \tau_{n+1}(\theta_s^n(\mu_s^n - Y_s^n)) + \sigma_s^{n+1}(\tau_{n+1})^{0.5} \text{randn},$$

where randn is a realisation of a normally distributed random variable with mean 0 and variance 1.

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