Simplified Cell Migration: Derivation of the Euler-Lagrange Equation

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Introduction

We will consider the derivation of a simplified model for cell movement and its associated Euler-Lagrange equation. In this model only one set of filaments is included. Moreover, the model is constrained by the fact that filaments (seen in Figure 1 in green) are inextensible. In our model we will include bending, adhesion and twisting energies. The position in 2D-space at a given time t, at a particular filament a at a given monomer s, is described by $G : [0, \infty) \times B \longrightarrow G(t, a, s) \in \mathbb{R}^2$, where $B = [-\pi,\ \pi] \times [-L,\ 0]$. Let us introduce the three energies we include in our simplified model.

We define the bending as follows:

$$U^{\mathrm{bnd}}(t) = \frac{k_B}{2} \int_B (\partial_s^2 G)^2 \, \mathrm{d}(a, s). \tag{0.1}$$

We account for curvature of a single filament by taking the second derivative with respect to s (particular monomer in time on a specific filament). To account for the entire curvature of all filaments we sum over all monomers and all filaments.

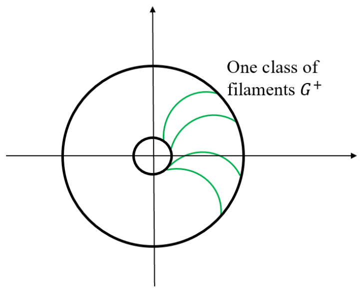


Figure 1: Schematic diagram of our model with one class of filaments: G^+

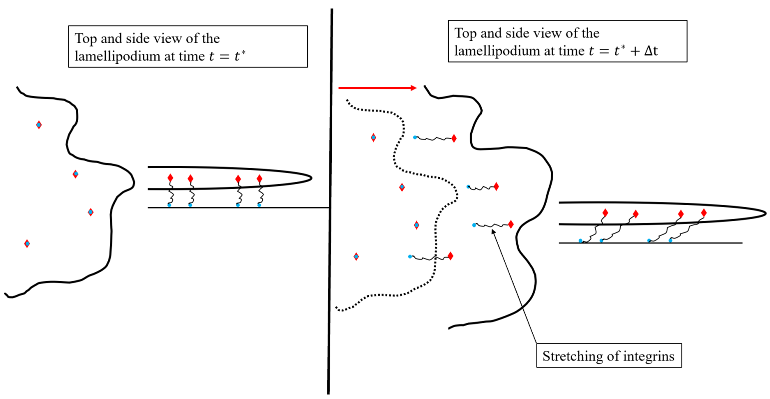
To capture the forces that arise due to the adhesion of integrins to the substrate we must consider the restoring forces that come into play as the lamellipodium (edge of cell) moves (see Figure 2). These are defined as:

$$U^{\mathrm{adh}}(t) = \frac{k_A}{2} \int_B \big(A(G)\big)^2 \, \mathrm{d}(a, s), \tag{0.2}$$

where

$$A(G) = \lim_{\Delta t \to 0} \left\{ G(t, a, s) - G\left(t - \Delta t, a, s + \int_{t-\Delta t}^{t} v(a, \tilde{t}) \, \mathrm{d}\tilde{t}\right) \right\}.$$

Above we also define the polymerisation rate which has speed v. Note that the associated material derivative is given as $A(G)A'(G) = D_t G$.



(a)

Figure 2: As the lamellipodium expands in time the integrins stretch. At the same time restoring forces try and pull them back (this is represented in the adhesion energy).

We lastly introduce the energy produced by filaments trying to twist back into their equilibrium configuration ϕ_0,

$$U^{\text{twist}}(t) = \frac{k_T}{2} \int_B T \left(\partial_s G\right)^2 \, \mathrm{d}(a,s), \tag{0.3}$$

with twisting defined as the difference of the measured angle, $\phi\left(\partial_s G\right)$ (from the horizontal axis), with ϕ_0 ($\approx 70°$):

$$T\left(\partial_s G\right) = \phi\left(\partial_s G\right) - \phi_0.$$

Recall the constraint placed, the in-extensibility of the filaments, mathematically represented as:

$$\left(\partial_s G\right)^2 = 1.$$

A further assumption made is that at $s = -L$ and $s = 0$ all quantities yield zero contributions.

Combining the energies (0.1), (0.2) and (0.3) we obtain the total energy in our system:

$$\begin{aligned} U^{\text{total}}(t) = \int_B & \frac{k_B}{2}(\partial_s^2 G)^2 + \frac{k_A}{2}\left(A(G)\right)^2 + \frac{k_T}{2}\left(\partial_s G\right)^2 \, \mathrm{d}(a,s) \\ & + \lambda\left(\left(\partial_s G\right)^2 - 1\right). \end{aligned}$$

The lamellipodium minimizes this energy and thus we take the variation to derive the PDE which the minimiser satisfies (where G' denotes $\partial_s G$):

$$\begin{aligned} \delta U = \int_B & \delta G \left(k_A A(G) A'(G)\right) + \delta G' \left(k_T T(\partial_s G) T'(\partial_s G) + 2\lambda \partial_s G\right) + \delta G'' \left(k_B \partial_s^2 G\right) \, \mathrm{d}(a,s) \\ & + \delta\lambda\left((\partial_s G)^2 - 1\right). \end{aligned}$$

In the derivation of the associated Euler-Lagrange equation we consider the terms premultiplying $\delta G'$ and $\delta G''$ separately.

Case $\delta G'$: Change $\delta G'$ to δG.

$$\begin{aligned} \int_B \delta G' \left(k_T T(\partial_s G) T'(\partial_s G) + 2\lambda \partial_s G\right) \, \mathrm{d}(a,s) = \int_B & \partial_s \left(\left(k_T T(\partial_s G) T'(\partial_s G) + 2\lambda \partial_s G\right)\delta G\right) \\ & - \partial_s \left(k_T T(\partial_s G) T'(\partial_s G) + 2\lambda \partial_s G\right)\delta G \, \mathrm{d}(a,s). \end{aligned}$$

Note that because of zero contributions at the boundary $s = -L, 0$ we find that the first contribution:

$$\begin{aligned} & \int_B \partial_s \left(\left(k_T T(\partial_s G) T'(\partial_s G) + 2\lambda \partial_s G\right)\delta G\right) \, \mathrm{d}(a,s) \\ & \quad = \int_{a=-\pi}^{\pi} \left(k_T T(\partial_s G) T'(\partial_s G) + 2\lambda \partial_s G\right)\delta G\Big|_{s=-L}^{0} \, \mathrm{d}a = 0 \end{aligned}$$

vanishes ($\delta G = 0$ at boundaries of s). Thus leaving us with

$$\int_B \delta G' \left(k_T T(\partial_s G) T'(\partial_s G) + 2\lambda \partial_s G\right) \, \mathrm{d}(a,s) = \int_B -\partial_s \left(k_T T(\partial_s G) T'(\partial_s G) + 2\lambda \partial_s G\right)\delta G \, \mathrm{d}(a,s).$$

Case $\delta G''$: change $\delta G''$ to δG.

$$\int_B \delta G'' \Big(k_B \partial_s^2 G \Big) \, \mathrm{d}(a,s) = \int_B \partial_s \Big((k_B \partial_s^2 G) \delta G' \Big) - \partial_s \Big(k_B \partial_s^2 G \Big) \delta G' \, \mathrm{d}(a,s).$$

Looking at the first contribution of the above right hand side integral:

$$\int_B \partial_s \Big((k_B \partial_s^2 G) \delta G' \Big) \, \mathrm{d}(a,s) = \int_{a=-\pi}^{\pi} (k_B \partial_s^2 G) \delta G' \Big|_{s=-L}^{0} \, \mathrm{d}a = 0,$$

recalling that all quantities vanish at the boundary of s ($\delta G' = 0$ at $s = -L, 0$). We have leftover:

$$\int_B \delta G'' \Big(k_B \partial_s^2 G \Big) \, \mathrm{d}(a,s) = - \int_B \partial_s \Big(k_B \partial_s^2 G \Big) \delta G' \, \mathrm{d}(a,s).$$

We now need to remove the derivative with respect to s from $\delta G'$:

$$\int_B -\partial_s \Big(k_B \partial_s^2 G \Big) \delta G' \, \mathrm{d}(a,s) = \int_B \partial_s \Big(-\partial_s (k_B \partial_s^2 G) \delta G \Big) - \partial_s \Big(-\partial_s (k_B \partial_s^2 G) \Big) \delta G \, \mathrm{d}(a,s).$$

We again observe that the first expression on the right hand side will vanish:

$$\int_B \partial_s \Big(-\partial_s (k_B \partial_s^2 G) \delta G \Big) \, \mathrm{d}(a,s) = \int_{a=-\pi}^{\pi} -\partial_s (k_B \partial_s^2 G) \delta G \Big|_{s=-L}^{0} \, \mathrm{d}a = 0,$$

leaving behind

$$\int_B -\partial_s \Big(-\partial_s (k_B \partial_s^2 G) \Big) \delta G \, \mathrm{d}(a,s) = \int_B \partial_s^2 (k_B \partial_s^2 G) \delta G \, \mathrm{d}(a,s) = \int_B k_B \partial_s^4 G \delta G \, \mathrm{d}(a,s).$$

The E-L equation

Combining all these expressions back into the total energy gives:

$$\begin{aligned} \delta U = \int_B \delta G \Big((k_A A(G) A'(G)) - \partial_s \Big(k_T T(\partial_s G) T'(\partial_s G) + 2\lambda \partial_s G \Big) + k_B \partial_s^4 G \Big) \, \mathrm{d}(a,s) \\ + \delta\lambda \left((\partial_s G)^2 - 1 \right). \end{aligned}$$

A minimizer of U satisfies $\delta U = 0$ giving rise to

$$\begin{aligned} \int_B \delta G \Big((k_A A(G) A'(G)) - \partial_s \Big(k_T T(\partial_s G) T'(\partial_s G) + 2\lambda \partial_s G \Big) + k_B \partial_s^4 G \Big) \, \mathrm{d}(a,s) \\ + \delta\lambda \left((\partial_s G)^2 - 1 \right) = 0 \ \forall \ \delta G, \ \delta\lambda. \end{aligned}$$

We have therefore have the Euler-Lagrange equation with the constraint:

$$\begin{aligned} & k_A \cdot D_t G - \partial_s \Big(k_T T(\partial_s G) T'(\partial_s G) + 2\lambda \partial_s G \Big) + k_B \partial_s^4 G = 0, \ \delta\lambda = 0, \\ & (\partial_s G)^2 - 1 = 0, \ \delta G = 0, \end{aligned}$$

where $T(\partial_s G) T'(\partial_s G) = (\phi(\partial_s G) - \phi_0)(\partial_s \phi \cdot \partial_s^2 G)$.