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The Filament Based Lamellipodium Model in the Limit of Short Filaments

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Abstract

One mathematical model for the dynamics of the actin filament network in the lamellipodium of migrating cells is the *Filament Based Lamellipodium Model* (FBLM) – a two-dimensional, anisotropic two-phase continuum model. In this thesis, we aim to propose a simplified version of this model, by considering rigid filaments of equal length. We then perform a formal asymptotic dimension reduction limit in the regime of small filaments. The resulting one-dimensional system describes the processes along the cell periphery.

Keywords: Actin, Cytoskeleton, Cell Movement, Mathematical Model.

Zusammenfassung

Ein mögliches mathematisches Modell für die Dynamik des Aktin-Netzes im Lamellipodium von kriechenden Zellen ist das *Filament Based Lamellipodium Model* (FBLM) – ein zweidimensionales, anisotropisches Zwei-Phasen-Modell. In dieser Arbeit wird eine vereinfachte Version dieses Modells vorgestellt, in der die Filamente als steif und gleicher Länge angenommen werden. Es wird ein formeller asymptotischer Dimensionsreduktionslimit durchgeführt, indem die Länge der Filamente gegen Null geführt wird. Das resultierende eindimensionale System beschreibt die Prozesse auf der Zellmembran.

Schlüsselwörter: Aktin, Cytoskelett, Zellbewegung, Mathematisches Modell.

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Introduction

Crawling is one of the most important cell activities in the animal kingdom, important in its generality and in its function.

- M. Abercrombie, 1978.¹

A central process in the development and maintenance of multicellular organisms is cell migration. It is crucial to numerous mechanisms in the animal body and its study is important to many fields of biology and medicine. For example, it contributes to many human medical conditions, such as vascular diseases or cancer, and insights into the happenings inside the cell would help to design therapies to counter these diseases.

So as it is very interesting as to why cells move, the research surrounding this thesis is dedicated to solve the question of "How". The cell organelle shouldering this responsibility is the cytoskeleton. Despite its name, it is not a static structure like the bone skeleton; in fact it is highly dynamic, continuously being remodeled. A network of so called actin filaments underlies the plasma membrane of a cell lying on a flat adhesive surface and experiments² suggest, that the necessary ingredients for cell movement lie in this thin strip, termed the lamellipodium.

One of many mathematical models to describe the dynamics in this cell protrusion is the Filament Based Lamellipodium Model (FBLM) – a two-dimensional, anisotropic, two-phase continuum model. The aim of this thesis is to derive a simplified one-dimensional version of it, which ideally yields the same results in the numerical simulations as the full model, but with lower computational costs. The first chapter is devoted to the presentation of the biological setting and the introduction of the FBLM. In the second chapter, some simplifying assumptions will be made and a formal asymptotic dimension reduction limit will be carried out.

¹[A78] ²[VSB99]

1 Framework

1.1 The Biological Concept³

Cell migration is an important part of cell biology, embryology, immunology and neuroscience as it is fundamental for development, tissue homeostasis and disease control. Embryogenesis, for example, requires the coordinated migration of cells to develop the right multicellular structure. Fibroblasts and epithelial cells are involved in wound closure. Immune cells leave the blood stream to reach their site of action. The advancing front of a growing axon cuts its way to the synapse. On the other hand, autoimmune diseases and tumor metastasis can be a consequence of deregulated cell motility.

Locomotion of cells takes place in fluid, on non-cellular substratum and around or even through other cells. Most animal cells move in a crawling motion, instead of swimming using cilia or flagella. One way to effect this is by protrusion of the front, attachment to the substratum, translocation of the cell body, and retraction of the rear. (The front-rear-polarity results from molecular and functional intracellular asymmetry which causes a morphological one.) These characteristic events occur consecutively in slowly moving cells, or simultaneously when cells move rapidly. In response to the cell's microenvironment the activation of multiple intertwined signaling networks is triggered, with numerous proteins participating: membrane receptors, signaling kinases, phosphatases, adapters and adhesion and cytoskeletal components.

1.1.1 The Cytoskeleton

For eukaryotic cells to organize their shape and internal structure and to stay sturdy and strong in form, as well as to interact mechanically with other cells, they possess three kinds of highly dynamic families of protein filaments spread across the whole cytoplasm, collectively called the cytoskeleton. These networks are attached to the plasma membrane and the internal organelles and have a spatial extent up to hundreds of micrometers and lifespans ranging from a few seconds up to the cell's lifetime. A coordinated interaction allows the cell to function properly during growth and division and to quickly adapt to changing circumstances.

The cytoskeletal proteins are categorized into intermediate filaments, microtubuli and

³Unless otherwise stated, the information in this section is mainly adapted from [A+05, A+15, L+12], where a more detailed description can be found.

actin filaments, each possessing its own characteristics and function. The intermediate filaments protect the DNA by enveloping the nucleus and play a vital role in the mechanical stability of a tissue by interacting with neighboring cells. Microtubuli form a transport system for vesicles, organelles and other components, providing the cell with an organized composition. They also form the spindle apparatus during mitosis, helping to separate the chromosome pairs. The third type, actin filaments, or microfilaments, function as tracks for motor proteins transporting cargo across the cell and as organizers of the plasma membrane, e.g. forming surface structures like microvilli. Since they are also primarily responsible for the motility of the cell, such as phagocytosis, mitosis and, especially, migration, we will pay them special attention.

1.1.2 Actin Filaments: Where Motility Begins

Actin makes up around 5% of a eukaryotic cell's protein pool; half of it as free globular monomers (G-actin), the other half in the form of filaments (F-actin), i.e. double helical chains of identical G-actins with a diameter of approximately 7 nm. Each G-actin is bound to a molecule of ATP (adenosine triphosphate) or ADP (adenosine diphosphate) and due to an uneven distribution of mass in its subdomains, it is considered to have a structural polarity. When reversibly polymerized head-to-tail into F-actin, all subunits point towards the same end, giving rise to a minus and a plus end, depending on whether the ATP⁴ binding site is exposed or not, respectively. From their arrow-like appearance when prepared with a certain "decoration" technique involving myosin⁵, one derives a different nomenclature: The minus end is also referred to as "pointed" and the plus end as "barbed".

Actin density is controlled by so-called polymerisation, branching, severing and capping processes, coordinated by multiple regulatory proteins, and resulting in a decreasing density from a cell's front to rear. A polymer is kept together by weak noncovalent bonds, allowing for rapid assembly and disassembly. So albeit the filaments diffuse only slowly, disassembling them into smaller - ergo more diffusive - components and reassembling them at another site, allows for rapid reorganization of the cytoskeleton. The filaments elongate by attaching monomers at both ends, with a higher probability at the plus/barbed end, whereas at the minus/pointed ends mostly decomposition occurs. The difference comes about due to the fact, that the subunits must be changed conformationally when added at the minus end.⁶ These processes are referred to as **polymerisation** and depolymerisation and count as major features of cell movement. New filaments emerge through branching or nucleation, old filaments can be severed and capped to protect against further uncontrolled de-/polymerisation, and stabilisation of the network is guaranteed by

⁴or ADP ⁵[BRR78] ⁶[A+02]

crosslinks. That is to say actin filaments are rarely found isolated; actin binding proteins bundle them or nucleate them into dendritic or gel-like networks.

Depending on the kind of proteins associated to the filaments, they can take over different tasks. The highest concentration is found in a phase directly adjacent to the plasma membrane, the cell cortex, where crosslinking proteins hold the actin filaments in a gelatinous mesh. This mesh stabilizes the outer edge of the cell and provides the basis for shape and motion.

Protrusion of the Front

On adhesive surfaces, at and near the front end (with respect to the direction of motion) - or leading edge - of cultured crawling cells, one observes "thin, sheet-like, mobile, commonly transitory projections"⁷, which Michael Abercrombie was the first to name "**lamellipodium**" in 1970. These are roughly 2 μm thick and 1-5 μm wide⁸ flexible structures, consisting mainly of actin; protruding and retracting in an exploratory manner.

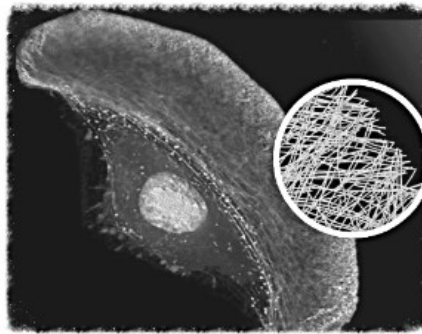


Fig. 1.1: Lamellipodium with actin filaments in a crawling keratocyte.

The force for the membrane deformation is provided by a certain mechanism called "**treadmilling**"⁹: a net flux of subunits through the polymer, while keeping it at constant length. This is where the above mentioned ATP comes in. Actin can catalyze the hydrolysis of ATP, at increased speed when assembled into filaments. A hydrogen atom takes the place of one phosphate group in the trinucleotide, changing the actin from "T form" (ATP bound) into "D form" (ADP bound), which is less stable and will therefore rather be depolymerised than polymerised. Whether the ends of a microfilament are in T or D form depends on the rate of polymerization: If it is higher than the rate of hydrolysis, than the end concerned will more likely still be in T form. At intermediate concentrations of free G-actin in the cytosol the plus end will be in T form (net growth), whereas the minus end will be in D form (net shrinkage at the same rate), effecting a steady state turnover of monomers whereby the length of the filament stays constant.

In the lamellipodium, the filaments are oriented with their fast growing plus ends

⁷[A70] ⁸[Sm+02] ⁹for details see [A+02]

abutting the membrane. Due to the treadmilling effect, monomers will be removed at the minus end near the center of the cell and inserted between the plus end and the membrane in the front. The free energy released during this spontaneous process is transformed into mechanical work: The elongation of the actin filaments pushes the leading edge forward, resulting in a progression at constant velocity of approximately 1 μm per second while the breadth of the lamellipodium remains constant.

Adhesion to the Substratum

After protrusion as described above and assembly of the cytoskeleton in the front of the cell have been accomplished, contractile microfilaments called stress fibers along the basal surface become firmly anchored to the underlying substratum via specialized regions called (focal) adhesions. This cell-cell or cell-matrix attachment is implemented by a myriad of cell surface proteins, called integrins. They have an external domain that binds stably to specific components of the extracellular matrix or the artificial surface, and a cytoplasmic domain which links to the cytoskeleton. The importance of this linkage becomes clear when regarding the following step.

Succeeding Steps in Cell Movement

Despite the focus of this thesis will be laid on protrusion via actin polymerisation and adhesion to the underlying surface, a short overview on the subsequent processes shall be given.

Translocation of the cell body. Adjacent to the highly dynamic lamellipodium one finds a more stable region, the lamella, where the concentration of the motor protein myosin II is increased. This is why it is believed, that the organelles are translocated by a myosin II mediated cortical contraction. Motor proteins are able to use energy released from ATP hydrolysis to generate mechanical work, i.e. linear or rotary motion. A myosin II molecule binds to two antiparallel actin filaments and walks towards their barbed ends, causing a contraction. The adhesion receptors allow the cell to transmit these forces to the substratum and prevent the leading edge from a phenomenon known as *retrograde flow*: The actin network would simply slip back inside the cytosol instead of pulling the cell body forwards.

Retraction of the rear. Next, the trailing edge of the cell must be retracted. This happens by breaking the rear adhesions and contraction of probably the stress fibers or microtubules.

Finally, recycling should be mentioned. Membrane constituents and adhesion molecules released at the rear of the cell can be incorporated into the advancing front.

Summing up, cell migration is a consequence of coordinated interaction of different components of the cytoskeleton and multiple other proteins, at the basis of balancing mechanical forces and resisting forces.

1.2 The Mathematical Model¹⁰

The history of modelling cell migration reaches back to around 1993 and covers microscopic as well as macroscopic continuum approaches. The operations on single filaments are typically described by stochastic processes, however these models are too complex to portray the mechanics of the whole lamellipodium. Instead, continuum versions for the filament network have been used. C.S. Peskin, G.M. Odell and G.F. Oster were among the first to introduce a mathematical model for this phenomenon: the Brownian ratchet [POO93]; soon revised by A. Mogilner and G.F. Oster [MO96]. In the subsequent years, many publications on the topic followed [AD98, MB01, GO04, RJM05, M+06, ...]. The underlying model of this thesis has its origins in publications of D. Oelz and C. Schmeiser of 2008 and 2010 [OSS08, OS10a]. It is a continuum model for the lamellipodium based on models for individual filaments of graded lengths together with their linkages, which allows to include detailed physical knowledge on the subprocesses.

1.2.1 The Constituent Elements

The model obeys the following assumptions:

The focus is laid on the processes in the front and rear of an isolated cell on a flat surface. Its membrane is modeled like a rubber band, which needs applied force to stretch it away from the equilibrium state. All filaments are required to meet the membrane with their barbed ends. Observations show, that the angle the filaments form with the membrane mainly takes two values, because of a branching angle of $\sim 70^\circ$. Therefore it is justified to speak of two families of locally parallel filaments, referred to as clockwise and anticlockwise, which cross each other transversally. The lamellipodium is assumed to be two dimensional since it is a very flat structure, and to surround the whole cell in the shape of a ring of varying width along the cell periphery. That means, the filaments lie between two closed curves: The outer defined by the leading edge, the inner rather artificially by the minimum density of actin, which is distinct for each of the two families, possibly non-identical. The actin filaments themselves are oriented, curved, inextensible segments, resistant to bending.

In the following, the position of the filaments of the two families will be given by the functions

$$\begin{aligned} F &: [0, 2\pi) \times [-L, 0] \times [0, \infty] \rightarrow \mathbb{R}^2 \\ F^* &: [0, 2\pi) \times [-L^*, 0] \times [0, \infty] \rightarrow \mathbb{R}^2, \end{aligned}$$

where $\alpha, \alpha^* \in [0, 2\pi)$ are the labels of the filaments, i.e. the positions of the attachments to the circular membrane; $s \in [-L(\alpha, t), 0]$ and $s^* \in [-L^*(\alpha^*, t), 0]$

¹⁰For a detailed derivation see [OS10a] and [M+15].

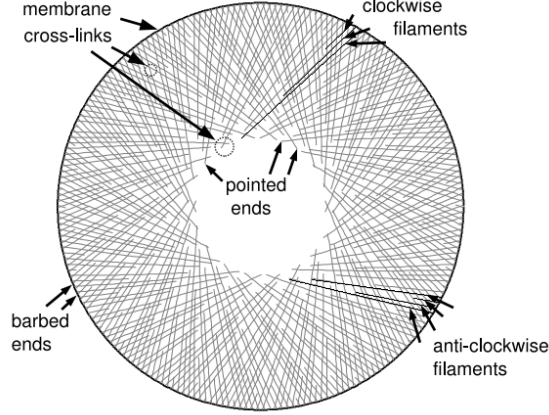


Fig. 1.2: Scheme of the idealized cell.

are the arclength parameters with maximal lengths L and L^* measured from the membrane; and $t \in [0, \infty]$ is the time.

Convention (C). The model is symmetric in the notion of $*$ and non- $*$. We make the following decision: The clockwise family will be denoted F^* and the anticlockwise family F . The filaments of both families will be labeled counterclockwise.

The **inextensibility condition** in mathematical terms states

$$|\partial_s F| = |\partial_s F^*| = 1. \quad (1.1)$$

This means that F and F^* represent arclength parametrizations, i.e. the deformation of all filaments in an infinitesimal α -, resp. α^* -interval with length distributions $\eta(\alpha, s, t), \eta^*(\alpha^*, s^*, t) \in [0, 1]$. These densities are monotonically nondecreasing in s and s^* resp. with their maximum in $s = 0$ and $s^* = 0$ resp.

Polymerisation occurs at the barbed ends with given speeds $v(\alpha, t), v^*(\alpha^*, t) \geq 0$, whereas depolymerization happens at the pointed ends in a stochastic manner with prescribed distribution. However, it should not be possible that the faster polymerizing family leaves the slower one behind. This condition is termed

$$\{F(\alpha, 0, t) : \alpha \in [0, 2\pi), t \in [0, \infty]\} = \{F^*(\alpha^*, 0, t) : \alpha^* \in [0, 2\pi), t \in [0, \infty]\}, \quad (1.2)$$

i.e. all filaments share the leading edge, which results in a pushing of the membrane by the fast family and a pulling by the slow family.

Filaments of the same family do not cross each other, which makes $F(\cdot, t)$ and $F^*(\cdot, t)$ one-to-one, whereas clockwise and anticlockwise filaments are elastically connected to each other at most once at any time by so-called crosslinks. They are formed stochastically and then move along the filaments until they eventually break. These crosslinking proteins ensure the stability of the network and possess an equilibrium

formation which causes a resistance against relative translational and rotational movement while attached.

Let $\mathcal{C}$ denote the set of index pairs of intersecting filaments:

$$\begin{aligned} \mathcal{C}(t) := \{(\alpha, \alpha^*) \in [0, 2\pi) \times [0, 2\pi) : \exists! s \in [-L, 0], s^* \in [-L^*, 0] \\ \text{s.t. } F(\alpha, s, t) = F^*(\alpha^*, s^*, t)\}. \end{aligned} \quad (1.3)$$

The uniqueness comes due to the fact, that two given filaments cross at most once. We define the function

$$a^* : [0, 2\pi) \times [-L, 0] \times [0, \infty) \rightarrow [0, 2\pi), \quad (1.4a)$$

such that $a^*(\alpha, s, t)$ is the index of the filament of the $*$ -family crossing filament α at location s and time t . Vice versa, the function

$$a : [0, 2\pi) \times [-L^*, 0] \times [0, \infty) \rightarrow [0, 2\pi) \quad (1.4b)$$

gives the crossing non- $*$ -filament for given α^* , s^* and t . Note that the two functions are inverse to each other for $s = s^* = 0$.

The angle between the filaments at the binding site is determined by

$$\varphi(\alpha, \alpha^*, t) = \arccos(\partial_s F(\alpha, s, t) \cdot \partial_{s^*} F^*(\alpha^*, s^*, t)) \in [0, \pi] \quad (1.5)$$

for $(\alpha, \alpha^*) \in \mathcal{C}$, with equilibrium φ_0 . Note that $\varphi = \varphi^*$, i.e. the angle is the same regardless of whether being measured from one filament or the other.

The elastic link between a filament and the substratum via a transmembrane linkage forms spontaneously and breaks depending on the degree of link extension. We suppose that the number of adhesions per filament length does not exceed a maximal value given as a parameter of the model.

1.2.2 The Filament Based Lamellipodium Model

Resistance against bending of the filaments, against stretching and twisting of the crosslinks, and against stretching of the adhesion linkages as well as of the cell membrane result in a balance of elastic forces. The minimum of the sum over all potential energy functionals of these elastic effects determine the time-dependent positions F of the filaments:

$$F = \min\{\text{potential energy functional containing contributions from elastic effects}\}$$

under the restraints (1.1),(1.2). This equation is coupled with age-structured population models for the contributions of the crosslinks and adhesions.

We suppose that cross-link's and adhesion's life times are small compared to the

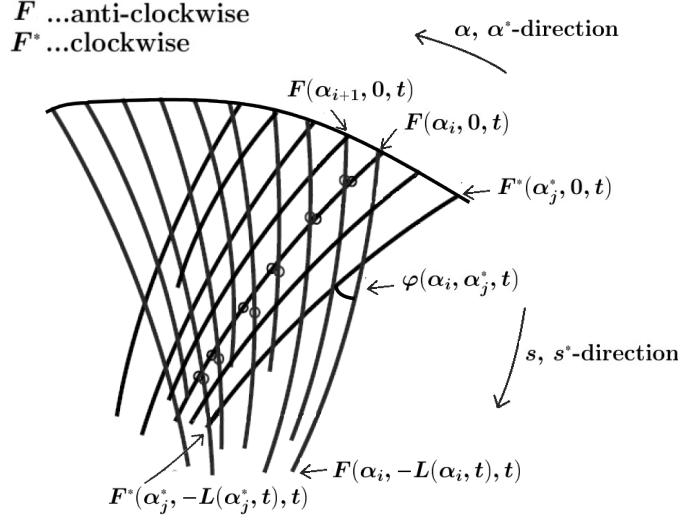


Fig. 1.3: Scheme of the constituent elements of the model.

time a monomer spends in the filament. As a consequence, their averaged effect is friction between the filaments and the substrate. (However, this is only justified for fast moving cells.) A limiting process and other techniques from variational calculus lead to a dimensionless two-dimensional model local in time, the **Filament Based Lamellipodium Model**. It is a two-phase model in which both families of filaments solve the following equation (the plus before the twisting term corresponds to the clockwise family, while the minus belongs to the counterclockwise family):

$$\begin{aligned}
 0 = & \underbrace{\mu^B \partial_s^2 (\eta \partial_s^2 F)}_{\text{bending}} + \underbrace{\mu^A \eta D_t F}_{\text{adhesion}} - \underbrace{\partial_s (\eta \lambda_{\text{inext}} \partial_s F)}_{\text{inextensibility}} \\
 & + \underbrace{\widehat{\mu^S} \eta \eta^* (D_t F - D_t^* F^*)}_{\text{cross-link stretching}} \pm \underbrace{\partial_s (\widehat{\mu^T} \eta \eta^* (\varphi - \varphi_0) \partial_s F^\perp)}_{\text{cross-link twisting}}
 \end{aligned} \tag{1.6}$$

where $\mu^B \in \mathbb{R}^+$ stiffness parameter

$\eta(\alpha, s, t) \in [0, 1]$ filament length density

$\mu^A \in \mathbb{R}^+$ adhesion coefficient

$D_t = \partial_t - v \partial_s$ material derivative

$\lambda_{\text{inext}}(\alpha, t) \in \mathbb{R}$ Lagrange multiplier, chosen s.t. (1.1) holds

$\varphi(\alpha, \alpha^*, t) \in [0, \pi]$ angle between two crossing filaments

$F^\perp = \begin{pmatrix} F_1 \\ F_2 \end{pmatrix}^\perp = \begin{pmatrix} -F_2 \\ F_1 \end{pmatrix}$ orthogonal vector.

Moreover in (1.6), the stiffness parameters of the cross-linking molecules are defined by

$$\widehat{\mu^S}(\alpha, s, t) = \begin{cases} \mu^S |\frac{\partial a^*}{\partial s}(\alpha, s, t)| & \text{whenever F crosses another filament} \\ 0 & \text{elsewhere,} \end{cases} \quad (1.7a)$$

where μ^S is the crosslink stretching constant, and

$$\widehat{\mu^T}(\alpha, s, t) = \begin{cases} \mu^T |\frac{\partial a^*}{\partial s}(\alpha, s, t)| & \text{whenever F crosses another filament} \\ 0 & \text{elsewhere,} \end{cases} \quad (1.7b)$$

where μ^T is the crosslink twisting constant.

Equation (1.6) is coupled with the condition that all filaments share the leading edge (1.2) and the **boundary conditions** read:

$$\begin{aligned} \mu^B \partial_s (\eta \partial_s^2 F) - \eta \lambda_{\text{inext}} \partial_s F \pm \widehat{\mu^T} \eta \eta^* (\varphi - \varphi_0) \partial_s F^\perp &= -f_0 & \text{for } s = 0 \\ \partial_s^2 F &= 0 \\ \mu^B \partial_s (\eta \partial_s^2 F) - \eta \lambda_{\text{inext}} \partial_s F \pm \widehat{\mu^T} \eta \eta^* (\varphi - \varphi_0) \partial_s F^\perp &= f_L & \text{for } s = -L, \\ \partial_s^2 F &= 0 \end{aligned} \quad (1.8)$$

where $f_0(\alpha, t)$, $f_L(\alpha, t)$ are linear forces at $s = 0, -L$ respectively. The pulling force on the inside of the cell is replaced by the requirement that the area of the cell stays constant, and can therefore be set to zero:

$$f_L(\alpha, t) = 0 \quad (1.9a)$$

$$f_L^*(\alpha^*, t) = 0. \quad (1.9b)$$

The force on the leading edge is then determined by this area constraint and that the families share the membrane. It will be chosen of order L – this choice will be justified in Section 2.1. We have

$$f_0(\alpha, t) = L(\alpha, t) \left(\lambda_{\text{tether}}(\alpha, t) + \frac{1}{2} \lambda_{\text{area}}(t) \right) \nu(\alpha, t) \quad (1.9c)$$

$$\begin{aligned} f_0^*(\alpha^*, t) &= L^*(\alpha^*, t) \left(\lambda_{\text{tether}}^*(\alpha^*, t) + \frac{1}{2} \lambda_{\text{area}}(t) \right) \nu^*(\alpha^*, t) \\ &= L^*(\alpha^*, t) \left(-\lambda_{\text{tether}}(a_0, t) \frac{\partial a}{\partial \alpha^*}(\alpha^*, 0, t) + \frac{1}{2} \lambda_{\text{area}}(t) \right) \nu(a_0, t), \end{aligned} \quad (1.9d)$$

where the abbreviation

$$a_0 =: a(\alpha^*, 0, t) \quad (1.10)$$

is used. The vector

$$\nu(\alpha, t) = -\frac{\partial_\alpha F_0^\perp(\alpha, t)}{|\partial_\alpha F_0^\perp(\alpha, t)|} \quad (1.11)$$

is the unit vector normal to the membrane pointing outwards. Note that $\nu^*(\alpha^*, t) = \nu(a(\alpha^*, 0, t), t)$ due to convention (C). The variable $\lambda_{\text{tether}}(\alpha, t) \in \mathbb{R}$ is the Lagrange multiplier to be chosen such that (1.2) holds and $\lambda_{\text{area}}(t) \in \mathbb{R}$ such that

$$A_0 = -\int_0^{2\pi} \frac{1}{2} F_0(\alpha, t) \cdot \partial_\alpha F_0^\perp(\alpha, t) d\alpha \quad (1.12)$$

is satisfied for given area $A_0 > 0$. It suffices to include the area constraint in one of the forces, since (1.2) ensures that the other family will behave accordingly, but we include it in both forces for symmetry reasons.

Sidenote on (1.9d): The derivative of a in the definition of $\lambda_{\text{tether}}^*$ has been forgotten in [OS10a, p.13]. See the appendix for the revision.

The FBLM is quasi-stationary, which means, that viscous forces in the cytosol damp the network such that elastic oscillations can be disregarded in the dynamics. And anisotropic, which means that the results are independent of the orientation of the filaments around the cell periphery. Although being very simplistic and not describing all relevant processes, it already gives quite a realistic simulation of a cell in motion. Several extensions and modifications to this model have been worked out in recent years. Geometric simplifications have been realised [OS10a, HMS16] and parameters have been varied. For branching, severing and capping processes, as well as pressure-like repulsion between the filaments, see [M+15]. The motor protein myosin has been introduced in [HMS16]. Numerical treatment including chemotaxis was treated in e.g. [M+16].

2 A Simplified Version of the FBLM

In this chapter, we aim to introduce more restrictive assumptions to develop a simpler version of the model. The filaments will be assumed to be rigid and of equal length with identical constant polymerization speeds. The limit of passing the filament length to zero will then be carried out formally.

(For reasons of clarity, the arguments of the functions will often be omitted, especially the time.)

2.1 The Assumption of Rigid Filaments¹¹

Actin filaments in the lamellipodium can be observed to be rather straight rods. This justifies the assumption of rigidity, which can be incorporated in the model through the limit of large bending stiffness: $\mu^B \rightarrow \infty$. The equation of the FBLM then becomes

$$0 = \partial_s^2(\eta \partial_s^2 F) \quad (2.1a)$$

under the boundary conditions

$$\partial_s^2 F = 0 \quad \text{for } s = 0, -L, \quad (2.1b)$$

the inextensibility condition (1.1), and the condition that all filaments share the leading edge (1.2).

Integration of the FBLM (1.6), using the boundary conditions (1.8), yields

$$\begin{aligned} 0 &= \int_{-L}^0 \mu^B \partial_s^2(\eta \partial_s^2 F) + \mu^A \eta D_t F - \partial_s(\eta \lambda_{\text{inext}} \partial_s F) \\ &\quad + \widehat{\mu^S} \eta \eta^*(D_t F - D_t^* F^*) \pm \partial_s(\widehat{\mu^T} \eta \eta^*(\varphi - \varphi_0) \partial_s F^\perp) \, ds \\ &= \left[\mu^B \partial_s(\eta \partial_s^2 F) - \eta \lambda_{\text{inext}} \partial_s F \pm \widehat{\mu^T} \eta \eta^*(\varphi - \varphi_0) \partial_s F^\perp \right]_{-L}^0 + \\ &\quad + \int_{-L}^0 \mu^A \eta D_t F + \widehat{\mu^S} \eta \eta^*(D_t F - D_t^* F^*) \, ds \\ &= -f_0 - f_L + \int_{-L}^0 \mu^A \eta D_t F + \widehat{\mu^S} \eta \eta^*(D_t F - D_t^* F^*) \, ds \end{aligned}$$

¹¹A continuation of [HMS16].

Including the boundary forces (1.9), we get the **total force balances**

$$L(\lambda_{\text{tether}} + \frac{1}{2}\lambda_{\text{area}})\nu = \int_{-L}^0 \mu^A \eta D_t F + \widehat{\mu^S} \eta \eta^* (D_t F - D_t^* F^*) ds \quad (2.2a)$$

$$L^*(\lambda_{\text{tether}}^* + \frac{1}{2}\lambda_{\text{area}})\nu^* = \int_{-L^*}^0 \mu^A \eta^* D_t^* F^* + \widehat{\mu_*^S} \eta^* \eta (D_t^* F^* - D_t F) ds^* \quad (2.2b)$$

for the two families respectively. Note that this remains valid in the limit of rigid filaments.

On the other hand, partial integration of the FBLM against $(F - F_0)^\perp$ using the boundary conditions (1.8) in the limit of rigid filaments yields

$$\begin{aligned} 0 &= \int_{-L}^0 (F - F_0)^\perp \cdot \left(\mu^B \partial_s^2 (\eta \partial_s^2 F) + \mu^A \eta D_t F - \partial_s (\eta \lambda_{\text{inext}} \partial_s F) \right. \\ &\quad \left. + \widehat{\mu^S} \eta \eta^* (D_t F - D_t^* F^*) \pm \partial_s (\widehat{\mu^T} \eta \eta^* (\varphi - \varphi_0) \partial_s F^\perp) \right) ds \\ &= \left[(F - F_0)^\perp \cdot \left(\mu^B \partial_s (\eta \partial_s^2 F) - \eta \lambda_{\text{inext}} \partial_s F \pm \widehat{\mu^T} \eta \eta^* (\varphi - \varphi_0) \partial_s F^\perp \right) \right]_{-L}^0 \\ &\quad - \int_{-L}^0 \partial_s (F - F_0)^\perp \cdot \left(\mu^B \partial_s (\eta \partial_s^2 F) - \eta \lambda_{\text{inext}} \partial_s F \pm \widehat{\mu^T} \eta \eta^* (\varphi - \varphi_0) \partial_s F^\perp \right) \\ &\quad + \int_{-L}^0 (F - F_0)^\perp \cdot \left(\mu^A \eta D_t F + \widehat{\mu^S} \eta \eta^* (D_t F - D_t^* F^*) \right) ds \\ &= (F - F_0)^\perp \Big|_{s=0} \cdot (-f_0) - (F - F_0)^\perp \Big|_{s=-L} \cdot f_L \mp \int_{-L}^0 \widehat{\mu^T} \eta \eta^* (\varphi - \varphi_0) ds \\ &\quad + \int_{-L}^0 (F - F_0)^\perp \cdot \left(\mu^A \eta D_t F + \widehat{\mu^S} \eta \eta^* (D_t F - D_t^* F^*) \right) ds \end{aligned}$$

which, together with (1.9), gives the **total torque balances**

$$\begin{aligned} (F - F_0)^\perp \Big|_{s=0} \cdot \nu L(\lambda_{\text{tether}} + \frac{1}{2}\lambda_{\text{area}}) &= + \int_{-L}^0 \widehat{\mu^T} \eta \eta^* (\varphi - \varphi_0) ds \\ &\quad + \int_{-L}^0 (F - F_0)^\perp \cdot \left(\mu^A \eta D_t F + \widehat{\mu^S} \eta \eta^* (D_t F - D_t^* F^*) \right) ds \end{aligned} \quad (2.3a)$$

$$\begin{aligned} (F^* - F_0^*)^\perp \Big|_{s^*=0} \cdot \nu^* L^*(\lambda_{\text{tether}}^* + \frac{1}{2}\lambda_{\text{area}}) &= - \int_{-L^*}^0 \widehat{\mu_*^T} \eta^* \eta (\varphi^* - \varphi_0) ds^* \\ &\quad + \int_{-L^*}^0 (F^* - F_0^*)^\perp \cdot \left(\mu^A \eta^* D_t^* F^* + \widehat{\mu_*^S} \eta^* \eta (D_t^* F^* - D_t F) \right) ds^* \end{aligned} \quad (2.3b)$$

for the two families respectively.

Ansatz. One ansatz for a solution to (2.1) is

$$F(\alpha, s, t) = F_0(\alpha, t) + (s - s_0(\alpha, t))d(\omega(\alpha, t)), \quad (2.4)$$

where F_0 is the unknown center of mass, the mean length s_0 is determined by

$$\int_{-L}^0 \eta(\alpha, s, t) (s - s_0(\alpha, t)) ds = 0$$

and $d(\omega) = \begin{pmatrix} \cos \omega \\ \sin \omega \end{pmatrix}$ is the direction according to the unknown cartesian angle $\omega : [0, 2\pi) \times [0, \infty] \rightarrow [0, 2\pi)$. Note that in the following $d(\omega(\alpha, t))$ will be abbreviated as $d(\alpha)$ and $d(\omega^*(\alpha^*, t)) = d^*(\alpha^*)$.

Simplifying assumptions. Under the assumption that all filaments have the same length $L(\alpha, t) = L = L^*(\alpha^*, t)$, the filament length density is constant $\eta \equiv 1 \equiv \eta^*$ and therefore $s_0 = -\frac{L}{2} = s_0^*$. The polymerization speeds of the filaments of the two families will be assumed constant and identical $v = v^*$.

Under these simplifications, the forces of the filaments acting on one another are symmetric. This leads to a cancelation of the interaction terms of the total force balances when the equations for the two families are summed. Note that the integration domain differs depending on whether the term in question affects just one family of filaments or both. If it affects just one family, such as the adhesion term, then it will be integrated over the whole length $[-L, 0]$. An interaction term on the other hand will be integrated over just that length, where the filaments actually intersect. This property is already implicit in the interaction parameters: (1.7) can also be written as

$$\widehat{\mu^{S,T}} = \mu^{S,T} \left| \frac{\partial a^*}{\partial s} \right| \mathbb{1}_{\{s \geq \tilde{s}(\alpha)\}} \quad \widehat{\mu_*^{S,T}} = \mu_*^{S,T} \left| \frac{\partial a}{\partial s^*} \right| \mathbb{1}_{\{s^* \geq \tilde{s}^*(\alpha^*)\}},$$

where $\tilde{s}$ and $\tilde{s}^*$ are the smallest s and s^* , i.e. the innermost points, where intersection occurs. Note that then

$$\begin{aligned} \int_{-L}^0 \widehat{\mu^S} ds &= \int_{-L}^0 \mu^S \left| \frac{\partial a^*}{\partial s} \right| \mathbb{1}_{\{s \geq \tilde{s}\}} ds & \int_{-L^*}^0 \widehat{\mu_*^S} ds^* &= \int_{-L}^0 \mu^S \left| \frac{\partial a}{\partial s^*} \right| \mathbb{1}_{\{s^* \geq \tilde{s}^*\}} ds^* \\ &= \int_0^{2\pi} \mu^S \mathbb{1}_{\{(\alpha, \alpha^*) \in \mathcal{C}\}} d\alpha^* & &= \int_0^{2\pi} \mu^S \mathbb{1}_{\{(\alpha, \alpha^*) \in \mathcal{C}\}} d\alpha, \end{aligned}$$

so (2.2) is equivalent to

$$\begin{aligned} L(\lambda_{\text{tether}} + \frac{1}{2}\lambda_{\text{area}})\nu &= \int_{-L}^0 \mu^A D_t F ds + \int_0^{2\pi} \mu^S \mathbb{1}_{\{(\alpha, \alpha^*) \in \mathcal{C}\}} (D_t F - D_t^* F^*) d\alpha^* \\ L(\lambda_{\text{tether}}^* + \frac{1}{2}\lambda_{\text{area}})\nu^* &= \int_{-L}^0 \mu^A D_t^* F^* ds^* + \int_0^{2\pi} \mu^S \mathbb{1}_{\{(\alpha, \alpha^*) \in \mathcal{C}\}} (D_t^* F^* - D_t F) d\alpha. \end{aligned}$$

Integrating the first equation over all α and the second one over all α^* and summing

the results, gives the global equation

$$\begin{aligned} \frac{L}{2} \lambda_{\text{area}} \int_0^{2\pi} \left(1 + \frac{\partial a^*}{\partial \alpha}(\alpha, 0)\right) \nu(\alpha) d\alpha \\ = \int_0^{2\pi} \int_{-L}^0 \mu^A D_t F ds d\alpha + \int_0^{2\pi} \int_{-L}^0 \mu^A D_t^* F^* ds^* d\alpha^*, \end{aligned}$$

since

$$\begin{aligned} \int_0^{2\pi} \lambda_{\text{tether}}^*(\alpha^*) \nu^*(\alpha^*) d\alpha^* &= \int_0^{2\pi} -\lambda_{\text{tether}}(a(\alpha^*, 0)) \frac{\partial a}{\partial \alpha^*}(\alpha^*, 0) \nu(a(\alpha^*, 0)) d\alpha^* \\ &= \int_0^{2\pi} -\lambda_{\text{tether}}(\alpha) \nu(\alpha) d\alpha, \end{aligned}$$

performing a change of variables $\alpha = a(\alpha^*, 0)$ using $a^{-1}(\alpha, 0) = \alpha^*(\alpha, 0)$. The interaction terms cancel as intended and also the choice of f_0 and f_0^* as in (1.9) turns out to be reasonable, since the orders match.

2.2 The Limit of Short Filaments

In comparison to the size of the cell, the filaments are very short. This motivates our next simplification: $L \rightarrow 0$. Although carried out explicitly only quite late in the calculations, some assumptions will be made along the way, which arise from what is expected to be valid in the limit.

2.2.1 The Integration Domain for Interaction Terms

In the setting of short rigid filaments, we aim to compute the lower bounds of the integration domains, $\tilde{s}$ and $\tilde{s}^*$. Two cases occur:

- a) If the $*$ -family is steeper, then there exist intersecting filaments of the other family on the whole length of the α -filament. Therefore the integration domain is the whole length $[-L, 0]$.
- b) If the non- $*$ -family is steeper, then there is a part, where there exist no intersecting filaments. Therefore the integration domain is just a part of the whole length, i.e. $[s(\alpha^*, -L), 0]$, with $s(\alpha^*, -L) \in [-L, 0]$.

Note that case a) for α is case b) for α^* .

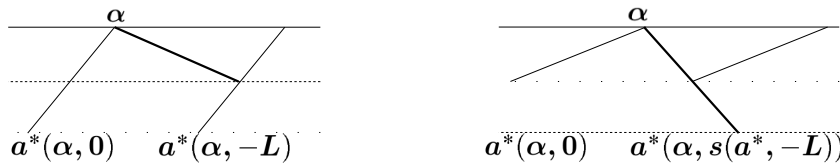


Fig. 2.1: Integration domain: case distinction. Left: case a), right: case b).

We will calculate $s(a^*, -L, t)$ in case b) using the law of sines. Assuming, that the membrane together with the two filaments build a triangle, is justified since the curvature of the membrane is small compared to the length of the filaments.

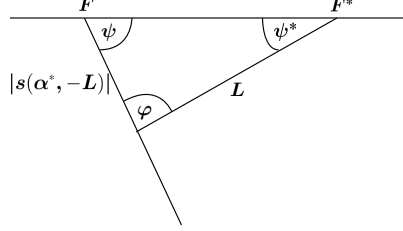


Fig. 2.2: Geometry.

Let $\psi(\alpha, t), \psi^*(\alpha^*, t)$ denote the angles to the membrane, as shown in Fig. 2.2. Then

$$\begin{aligned} \frac{\sin \psi}{L} &= \frac{\sin \psi^*}{|s(\alpha^*, -L)|} \\ \Leftrightarrow |s(\alpha^*, -L)| &= L \frac{\sin \psi^*}{\sin \psi} \\ &= L \frac{\partial_\alpha F_0(\alpha, t) \cdot d^{*\perp}(a^*(\alpha, -s(\alpha^*, -L), t))}{\partial_\alpha F_0(\alpha, t) \cdot d^\perp(\alpha)} \in [0, L], \end{aligned}$$

using the geometric definition of the scalar product and the fact that d is normalized. To cover both cases a) and b) in the integration, it is expedient to take the minimum of $-L$ and $s(\alpha^*, -L)$ as the lower bound of the s -intervall of crossing filaments:

$$\tilde{s}(\alpha, t) := -L \min \left\{ \frac{\partial_\alpha F_0(\alpha, t) \cdot d^{*\perp}(a^*(\alpha, -s(\alpha^*, -L), t))}{\partial_\alpha F_0(\alpha, t) \cdot d^\perp(\alpha)}, 1 \right\}. \quad (2.5a)$$

Analogously, for the other family:

$$\begin{aligned} \tilde{s}^*(\alpha^*, t) &:= -L \min \left\{ \frac{\sin \psi}{\sin \psi^*}, 1 \right\} \\ &= -L \min \left\{ \frac{\partial_{\alpha^*} F_0^*(\alpha^*, t) \cdot d^\perp(a(\alpha^*, -s^*(\alpha^*, -L), t))}{\partial_{\alpha^*} F_0^*(\alpha^*, t) \cdot d^{*\perp}(\alpha^*)}, 1 \right\}. \end{aligned} \quad (2.5b)$$

Note that $\tilde{s}, \tilde{s}^* \in [-L, 0]$ and that there are only three possible combinations of values for $\tilde{s}$ and $\tilde{s}^*$ – at least one of the two equals $-L$.

2.2.2 The Total Force and Total Torque Balances

For the substitution of the ansatz (2.4) into (2.2) and (2.3), we compute

$$\begin{aligned} D_t F &= (\partial_t - v \partial_s)(F_0 + (s + \frac{L}{2})d) = \partial_t F_0 + (s + \frac{L}{2})\partial_t d - v d \\ D_t^* F^* &= D_t F^* = (\partial_t - v \partial_s)(F_0^* + (s^* + \frac{L}{2})d^*) = \partial_t F_0^* + (s^* + \frac{L}{2})\partial_t d^* - v d^*. \end{aligned}$$

Note that $\frac{\partial a}{\partial s^*} \leq 0$ and $\frac{\partial a^*}{\partial s} \geq 0$ as a consequence of convention (C).

Considering all the preceding findings and simplifications, we get

$$\begin{aligned} L(\lambda_{\text{tether}} + \frac{1}{2}\lambda_{\text{area}})\nu &= \mu^A \int_{-L}^0 \partial_t F_0 + (s + \frac{L}{2})\partial_t d - vd \, ds \\ &\quad + \mu^S \int_{\tilde{s}}^0 \frac{\partial a^*}{\partial s} \left(\partial_t F_0 + (s + \frac{L}{2})\partial_t d - vd \right) ds \\ &\quad - \mu^S \int_{\tilde{s}}^0 \frac{\partial a^*}{\partial s} \left(\partial_t F_0^* + (s^* + \frac{L}{2})\partial_t d^* - vd^* \right) ds \end{aligned} \quad (2.6a)$$

$$\begin{aligned} L(\lambda_{\text{tether}}^* + \frac{1}{2}\lambda_{\text{area}})\nu^* &= \mu^A \int_{-L}^0 \partial_t F_0^* + (s^* + \frac{L}{2})\partial_t d^* - vd^* \, ds^* \\ &\quad - \mu^S \int_{\tilde{s}^*}^0 \frac{\partial a}{\partial s^*} \left(\partial_t F_0^* + (s^* + \frac{L}{2})\partial_t d^* - vd^* \right) ds^* \\ &\quad + \mu^S \int_{\tilde{s}^*}^0 \frac{\partial a}{\partial s^*} \left(\partial_t F_0 + (s + \frac{L}{2})\partial_t d - vd \right) ds^* \end{aligned} \quad (2.6b)$$

for the total force, and

$$\begin{aligned} \frac{L^2}{2}(\lambda_{\text{tether}} + \frac{1}{2}\lambda_{\text{area}})d^\perp \cdot \nu &= -\mu^T \int_{\tilde{s}}^0 \frac{\partial a^*}{\partial s} (\varphi - \varphi_0) \, ds \\ &\quad + \mu^A \int_{-L}^0 (s + \frac{L}{2})d^\perp \cdot \left(\partial_t F_0 + (s + \frac{L}{2})\partial_t d - vd \right) ds \\ &\quad + \mu^S \int_{\tilde{s}}^0 (s + \frac{L}{2})\frac{\partial a^*}{\partial s} d^\perp \cdot \left(\partial_t F_0 + (s + \frac{L}{2})\partial_t d - vd \right) ds \\ &\quad - \mu^S \int_{\tilde{s}}^0 (s + \frac{L}{2})\frac{\partial a^*}{\partial s} d^\perp \cdot \left(\partial_t F_0^* + (s^* + \frac{L}{2})\partial_t d^* - vd^* \right) ds \end{aligned} \quad (2.7a)$$

$$\begin{aligned} \frac{L^2}{2}(\lambda_{\text{tether}}^* + \frac{1}{2}\lambda_{\text{area}})d^{*\perp} \cdot \nu^* &= +\mu^T \int_{\tilde{s}^*}^0 \frac{\partial a}{\partial s^*} (\varphi - \varphi_0) \, ds^* \\ &\quad + \mu^A \int_{-L}^0 (s^* + \frac{L}{2})d^{*\perp} \cdot \left(\partial_t F_0^* + (s^* + \frac{L}{2})\partial_t d^* - vd^* \right) ds^* \\ &\quad - \mu^S \int_{\tilde{s}^*}^0 (s^* + \frac{L}{2})\frac{\partial a}{\partial s^*} d^{*\perp} \cdot \left(\partial_t F_0^* + (s^* + \frac{L}{2})\partial_t d^* - vd^* \right) ds^* \\ &\quad + \mu^S \int_{\tilde{s}^*}^0 (s^* + \frac{L}{2})\frac{\partial a}{\partial s^*} d^{*\perp} \cdot \left(\partial_t F_0 + (s + \frac{L}{2})\partial_t d - vd \right) ds^* \end{aligned} \quad (2.7b)$$

for the total torque.

2.2.3 Derivation of the Equations

To be able to carry out the integrations and to pass to the limit of $L \rightarrow 0$, the functions which depend on the integration variable will be expanded around zero. Reminder: We have seven unknowns: the two positions F_0, F_0^* , the two angles ω, ω^* ,

the Lagrange multipliers $\lambda_{\text{tether}}, \lambda_{\text{area}}$ and the function a^* that relates (α^*, s^*, t) to (α, s, t) . Therefore we need seven equations in dependency of the givens (α, t) . We also want those equations for matching F and F^* , i.e. those which cross. In particular those which cross in zero, because the functions a and a^* are inverse to each other in zero. We fix α and choose α^* such that $a(\alpha^*, 0, t) = \alpha$. This particular α^* will be denoted a_0^* and by definition we have

$$a_0^* = a^*(\alpha, 0, t). \quad (2.8)$$

Hence we will expand all the $*$ -functions in (2.6a, 2.7a) around $s = 0$:

$$\begin{aligned} \frac{\partial a^*}{\partial s}(\alpha, s, t) &= \frac{\partial a^*}{\partial s}(\alpha, 0, t) + O(L) \\ F_0^*(a^*(\alpha, s, t), t) &= F_0^*(a^*(\alpha, 0, t), t) + O(L) \\ d(\omega^*(a^*(\alpha, s, t), t)) &= d(\omega^*(a^*(\alpha, 0, t), t)) + O(L) \\ \varphi(\alpha, a^*(\alpha, s, t), t) &= \varphi(\alpha, a^*(\alpha, 0, t), t) + O(L), \end{aligned}$$

and analogously all non- $*$ -functions in (2.6b, 2.7b) around $s^* = 0$.

The first final equation can be directly drawn from (1.2). In the limit we have an **equation for F_0^*** :

$$F_0^*(a^*(\alpha, 0, t), t) = F_0(\alpha, t). \quad (2.9)$$

Put another way, this reads

$$F_0^*(\alpha^*, t) = F_0(a(\alpha^*, 0, t), t),$$

from which it follows

$$\partial_{\alpha^*} F_0^*(a^*(\alpha, 0, t), t) = \frac{\partial a}{\partial \alpha^*}(a^*(\alpha, 0, t), 0, t) \partial_{\alpha} F_0(\alpha, t) \quad (2.10)$$

$$\partial_t F_0^*(a^*(\alpha, 0, t), t) = \partial_t F_0(\alpha, t) + \frac{\partial a}{\partial t}(a^*(\alpha, 0, t), 0, t) \partial_{\alpha} F_0(\alpha, t). \quad (2.11)$$

Drawing Information from the Ansatz

First, we take a closer look at what's behind the derivatives $\frac{\partial a^*}{\partial s}$ and $\frac{\partial a}{\partial s^*}$. Their absolute values stand for the number of crossings per unit length. At the intersection point of two filaments, the following relation holds:

$$F_0(\alpha, t) + (s + \frac{L}{2})d(\omega(\alpha, t)) = F_0^*(a^*(\alpha, s, t), t) + (s^* + \frac{L}{2})d(\omega^*(a^*(\alpha, s, t), t)).$$

Taking the scalar product with $d^{*\perp}$ yields

$$\left(F_0 - F_0^* + (s + \frac{L}{2})d\right) \cdot d^{*\perp} = 0,$$

and deriving with respect to s gives

$$\left(-\partial_{\alpha^*} F_0^* \frac{\partial a^*}{\partial s} + d\right) \cdot d^{*\perp} + \left(F_0 - F_0^* + \left(s + \frac{L}{2}\right)d\right) \cdot \frac{dd}{d\omega^*} \frac{\partial \omega^*}{\partial \alpha^*} \frac{\partial a^*}{\partial s} = 0.$$

Therefore,

$$\frac{\partial a^*}{\partial s}(\alpha, s, t) = \frac{d(\alpha) \cdot d^{*\perp}(a^*(\alpha, s, t)) + O(L)}{\partial_{\alpha^*} F_0^*(a^*(\alpha, s, t), t) \cdot d^{*\perp}(a^*(\alpha, s, t))},$$

and analogously,

$$\frac{\partial a}{\partial s^*}(\alpha^*, s^*, t) = \frac{d^*(\alpha^*) \cdot d^\perp(a(\alpha^*, s, t)) + O(L)}{\partial_{\alpha} F_0(a(\alpha^*, s, t), t) \cdot d^\perp(a(\alpha^*, s, t))}.$$

With (2.10), the above equations can be written in the corresponding labels just in terms of (α, t) and evaluated in $s = s^* = 0$:

$$\frac{\partial a^*}{\partial s}(\alpha, 0, t) = \frac{\frac{\partial a^*}{\partial \alpha}(\alpha, 0, t) d(\omega(\alpha, t)) \cdot d^\perp(\omega^*(a_0^*, t))}{\partial_{\alpha} F_0(\alpha, t) \cdot d^\perp(\omega^*(a_0^*, t))} \quad (2.12a)$$

$$\frac{\partial a}{\partial s^*}(a_0^*, 0, t) = \frac{d(\omega^*(a_0^*, t)) \cdot d^\perp(\omega(\alpha, t))}{\partial_{\alpha} F_0(\alpha, t) \cdot d^\perp(\omega(\alpha, t))}. \quad (2.12b)$$

Remark: That the denominator does not become zero is ensured by the general prerequisite of the model, that the filaments are not allowed to be parallel to the leading edge.

Drawing Information from the Modified Total Torque Balances

In the lowest order of (2.7a) we have the twisting term:

$$0 = \mu^T \int_{\tilde{s}}^0 \frac{\partial a^*}{\partial s}(\alpha, s, t) (\varphi(\alpha, a^*(\alpha, s, t), t) - \varphi_0) ds + O(L^2).$$

With the above expansions, this yields

$$0 = \mu^T \tilde{s} \left(\frac{\partial a^*}{\partial s} \Big|_{s=0} (\varphi|_{s=0} - \varphi_0) \right) + O(L^2),$$

where $\tilde{s} = O(L)$. Dividing by L and passing to the limit, it follows

$$0 = \mu^T M \frac{\partial a^*}{\partial s} \Big|_{s=0} (\varphi|_{s=0} - \varphi_0)$$

with $M := \lim_{L \rightarrow 0} \frac{\tilde{s}}{L} = O(1)$, which means

$$\varphi(\alpha, a^*(\alpha, 0, t), t) = |\omega(\alpha, t) - \omega^*(a^*(\alpha, 0, t), t)| = \varphi_0.$$

From convention (C), this results in a **constraint for the angle ω^*** :

$$\omega^*(a^*(\alpha, 0, t), t) = \omega(\alpha, t) + \varphi_0. \quad (2.13)$$

Therefore, we know that

$$d^*(a_0^*) = d(\omega^*(a^*(\alpha, 0, t), t)) = d(\omega(\alpha, t) + \varphi_0).$$

To get information from the second order terms, we take the weighted sum of (2.7a) and (2.7b), such that the first order twisting term cancels. For this, the equations have to be written in the corresponding labels, i.e. for fixed α we choose $\alpha^* = a_0^*$. The weight for (2.7b) shall be the fraction of the two twisting terms:

$$\Phi(\alpha, t) := - \frac{\int_{\tilde{s}(\alpha, t)}^0 \frac{\partial a^*}{\partial s}(\alpha, s, t) (\varphi(\alpha, a^*(\alpha, s, t), t) - \varphi_0) ds}{\int_{\tilde{s}^*(a_0^*, t)}^0 \frac{\partial a}{\partial s^*}(a_0^*, s^*, t) (\varphi(a(a_0^*, s^*, t), a_0^*, t) - \varphi_0) ds^*} \geq 0.$$

Expanding the densities and φ , we get

$$\begin{aligned} \Phi(\alpha, t) &= - \frac{\tilde{s}(\alpha, t) \frac{\partial a^*}{\partial s}(\alpha, 0, t) (\varphi(\alpha, a_0^*, t) - \varphi_0) + O(L^2)}{\tilde{s}^*(a_0^*, t) \frac{\partial a}{\partial s^*}(a_0^*, 0, t) (\varphi(a(a_0^*, t), a_0^*, t) - \varphi_0) + O(L^2)} \\ &= \frac{\tilde{s}(\alpha, t) \frac{\partial a^*}{\partial \alpha}(\alpha, 0, t) \partial_\alpha F_0(\alpha, t) \cdot d^\perp(\omega(\alpha, t))}{\tilde{s}^*(a_0^*, t) \frac{\partial a}{\partial \alpha}(a_0^*, 0, t) \partial_\alpha F_0(a_0^*, 0, t) \cdot d^\perp(\omega(a_0^*, t) + \varphi_0)}, \end{aligned}$$

using equation (2.13) for the angle ω^* . For $L \rightarrow 0$ this converges to

$$\Phi_0(\alpha, t) := \frac{M(\alpha, t) \frac{\partial a^*}{\partial \alpha}(\alpha, 0, t) \partial_\alpha F_0(\alpha, t) \cdot d^\perp(\omega(\alpha, t))}{M^*(\alpha, t) \frac{\partial a}{\partial \alpha}(a_0^*, 0, t) \partial_\alpha F_0(a_0^*, 0, t) \cdot d^\perp(\omega(a_0^*, t) + \varphi_0)}, \quad (2.14)$$

where

$$M(\alpha, t) := \lim_{L \rightarrow 0} \frac{\tilde{s}(\alpha, t)}{L} = - \min \left\{ \frac{\partial_\alpha F_0(\alpha, t) \cdot d^\perp(\omega(\alpha, t) + \varphi_0)}{\partial_\alpha F_0(\alpha, t) \cdot d^\perp(\omega(\alpha, t))}, 1 \right\} \quad (2.15a)$$

$$M^*(\alpha, t) := \lim_{L \rightarrow 0} \frac{\tilde{s}^*(a_0^*, t)}{L} = - \min \left\{ \frac{\partial_\alpha F_0(a_0^*, t) \cdot d^\perp(\omega(a_0^*, t))}{\partial_\alpha F_0(a_0^*, t) \cdot d^\perp(\omega(a_0^*, t) + \varphi_0)}, 1 \right\}. \quad (2.15b)$$

Note that $M, M^* \in [-1, 0]$ and at least one of them equals -1 . The relation (2.10) was used to write the derivative in (2.15b) just in terms of (α, t) .

Depending on the values of M and M^* , the function Φ_0 simplifies to

$$\Phi_0 = \begin{cases} \frac{\partial a^*}{\partial \alpha}(\alpha, 0) \frac{\partial_\alpha F_0 \cdot d^\perp(\omega)}{\partial_\alpha F_0 \cdot d^\perp(\omega + \varphi_0)} & \text{if } M = M^* = -1 \\ \frac{\partial a^*}{\partial \alpha}(\alpha, 0) & \text{else.} \end{cases} \quad (2.16)$$

On the left hand side of (2.7a)+ Φ (2.7b), we have

$$\begin{aligned} & \frac{L^2}{2} \left((\lambda_{\text{tether}}(\alpha) + \frac{1}{2}\lambda_{\text{area}})(d^\perp(\alpha) \cdot \nu(\alpha)) \right. \\ & \quad \left. + \Phi(\alpha)(\lambda_{\text{tether}}^*(a_0^*) + \frac{1}{2}\lambda_{\text{area}})(d^{*\perp}(a_0^*) \cdot \nu^*(a_0^*)) \right) \\ &= \frac{L^2}{2} \left((\lambda_{\text{tether}}(\alpha) + \frac{1}{2}\lambda_{\text{area}})(d^\perp(\alpha) \cdot \nu(\alpha)) \right. \\ & \quad \left. + \Phi(\alpha) \left(-\lambda_{\text{tether}}(\alpha) \frac{\partial a}{\partial \alpha^*}(a_0^*, 0) + \frac{1}{2}\lambda_{\text{area}}(d^{*\perp}(a_0^*) \cdot \nu(\alpha)) \right) \right). \end{aligned}$$

On the right hand side, the adhesion term is of order 3 and can be disregarded. The summed stretching term reads

$$\begin{aligned} & \mu^S \int_{\tilde{s}}^0 \left(s + \frac{L}{2} \right) \frac{\partial a^*}{\partial s} d^\perp \cdot \left(\partial_t F_0 + \left(s + \frac{L}{2} \right) \partial_t d - vd - \partial_t F_0^*(a_0^*) \right. \\ & \quad \left. - \left(s^* + \frac{L}{2} \right) \partial_t d^*(a_0^*) + vd^*(a_0^*) \right) ds + \Phi \mu^S \int_{\tilde{s}^*(a_0^*)}^0 \left(s^* + \frac{L}{2} \right) \frac{\partial a}{\partial s^*}(a_0^*, s^*) d^{*\perp}(a_0^*) \\ & \quad \cdot \left(\partial_t F_0 + \left(s + \frac{L}{2} \right) \partial_t d - vd - \partial_t F_0^*(a_0^*) - \left(s^* + \frac{L}{2} \right) \partial_t d^*(a_0^*) + vd^*(a_0^*) \right) ds^* \\ &= \mu^S \left[\left(\int_{\tilde{s}(\alpha)}^0 \left(s + \frac{L}{2} \right) ds \right) \frac{\partial a^*}{\partial s}(\alpha, 0) d^\perp + \Phi \left(\int_{\tilde{s}^*(a_0^*)}^0 \left(s^* + \frac{L}{2} \right) ds^* \right) \frac{\partial a}{\partial s^*}(a_0^*, 0) d^{*\perp}(a_0^*) \right] \\ & \quad \cdot \left[\partial_t F_0 - vd - \partial_t F_0^*(a_0^*) + vd^*(a_0^*) \right] + O(L^3). \end{aligned}$$

The integrals solve to

$$\begin{aligned} \int_{\tilde{s}(\alpha)}^0 \left(s + \frac{L}{2} \right) ds &= - \left(\frac{\tilde{s}(\alpha)^2}{2} + \frac{L}{2} \tilde{s}(\alpha) \right) \\ \int_{\tilde{s}^*(a_0^*)}^0 \left(s^* + \frac{L}{2} \right) ds^* &= - \left(\frac{\tilde{s}^*(a_0^*)^2}{2} + \frac{L}{2} \tilde{s}^*(a_0^*) \right) \end{aligned}$$

and using (2.11), the total equation (2.7a)+ Φ (2.7b) reads

$$\begin{aligned} & \frac{L^2}{2} \left((\lambda_{\text{tether}} + \frac{1}{2}\lambda_{\text{area}})(d^\perp \cdot \nu) + \Phi \left(\frac{1}{2}\lambda_{\text{area}} - \lambda_{\text{tether}} \frac{\partial a}{\partial \alpha^*}(a_0^*, 0) \right) (d^{*\perp}(a_0^*) \cdot \nu) \right) \\ &= \mu^S \left[v(d - d^*(a_0^*)) + \frac{\partial a}{\partial t}(a_0^*, 0) \partial_\alpha F_0 \right] \cdot \left[\left(\frac{\tilde{s}(\alpha)^2}{2} + \frac{L}{2} \tilde{s}(\alpha) \right) \frac{\partial a^*}{\partial s}(\alpha, 0) d^\perp \right. \\ & \quad \left. + \Phi \left(\frac{\tilde{s}^*(a_0^*)^2}{2} + \frac{L}{2} \tilde{s}^*(a_0^*) \right) \frac{\partial a}{\partial s^*}(a_0^*, 0) d^{*\perp}(a_0^*) \right] + O(L^3) \\ &= O(L^3) + \mu^S \left[\frac{\partial a^*}{\partial s}(\alpha, 0) \left(\frac{\tilde{s}^2}{2} + \frac{L}{2} \tilde{s} \right) d^\perp \cdot \left(\frac{\partial a}{\partial t}(a_0^*, 0) \partial_\alpha F_0 - vd^*(a_0^*) \right) \right. \\ & \quad \left. + \Phi \frac{\partial a}{\partial s^*}(a_0^*, 0) \left(\frac{\tilde{s}^*(a_0^*)^2}{2} + \frac{L}{2} \tilde{s}^*(a_0^*) \right) d^{*\perp}(a_0^*) \cdot \left(\frac{\partial a}{\partial t}(a_0^*, 0) \partial_\alpha F_0 + vd \right) \right] \end{aligned}$$

Dividing by $\frac{L^2}{2}$ and passing to the limit $L \rightarrow 0$, using the equation for ω^* (2.13) and

the definition (2.14), we obtain an algebraic **equation for the angle ω** :

$$\begin{aligned} & (\lambda_{\text{tether}} + \frac{1}{2}\lambda_{\text{area}})(d^\perp(\omega) \cdot \nu) + \Phi_0\left(\frac{1}{2}\lambda_{\text{area}} - \lambda_{\text{tether}}\frac{\partial a}{\partial \alpha^*}(a_0^*, 0)\right)(d^\perp(\omega + \varphi_0) \cdot \nu) \\ &= \mu^S \left[\frac{\partial a^*}{\partial s}(\alpha, 0)(M^2 + M)d^\perp(\omega) \cdot \left(\frac{\partial a}{\partial t}(a_0^*, 0)\partial_\alpha F_0 - vd(\omega + \varphi_0)\right) \right. \\ & \quad \left. + \Phi_0\frac{\partial a}{\partial s^*}(a_0^*, 0)(M^{*2} + M^*)d^\perp(\omega + \varphi_0) \cdot \left(\frac{\partial a}{\partial t}(a_0^*, 0)\partial_\alpha F_0 + vd(\omega)\right) \right]. \end{aligned} \quad (2.17)$$

Drawing Information from the Modified Total Force Balances

Integration of the adhesion term of (2.6a) with respect to s gives

$$\begin{aligned} \mu^A \int_{-L}^0 \partial_t F_0 + (s + \frac{L}{2})\partial_t d - vd \, ds &= \mu^A \left(L(\partial_t F_0 - vd) + \partial_t d \int_{-L}^0 (s + \frac{L}{2}) \, ds \right) \\ &= \mu^A L(\partial_t F_0 - vd). \end{aligned}$$

The first part of the stretching term results in

$$\mu^S \int_{\tilde{s}}^0 \frac{\partial a^*}{\partial s} \left(\partial_t F_0 + (s + \frac{L}{2})\partial_t d - vd \right) ds = \mu^S \tilde{s} \frac{\partial a^*}{\partial s} \Big|_{s=0} (\partial_t F_0 - vd) + O(L^2)$$

and the second part gives

$$\begin{aligned} & -\mu^S \int_{\tilde{s}}^0 \frac{\partial a^*}{\partial s} \left(\partial_t F_0^* + (s^* + \frac{L}{2})\partial_t d^* - vd^* \right) ds \\ &= -\mu^S \tilde{s} \frac{\partial a^*}{\partial s} \Big|_{s=0} (\partial_t F_0^* \Big|_{s=0} - vd^* \Big|_{s=0}) + O(L^2). \end{aligned}$$

Altogether, we deduce

$$\begin{aligned} L(\lambda_{\text{tether}} + \frac{1}{2}\lambda_{\text{area}})\nu &= \mu^A L(\partial_t F_0 - vd) \\ &+ \mu^S \tilde{s} \frac{\partial a^*}{\partial s} \Big|_{s=0} (\partial_t F_0 - vd - \partial_t F_0^* \Big|_{s=0} + vd^* \Big|_{s=0}) + O(L^2) \end{aligned}$$

for one family and analogously from (2.6b)

$$\begin{aligned} L(\lambda_{\text{tether}}^* + \frac{1}{2}\lambda_{\text{area}})\nu^* &= \mu^A L(\partial_t F_0^* - vd^*) \\ &- \mu^S \tilde{s}^* \frac{\partial a}{\partial s^*} \Big|_{s^*=0} (\partial_t F_0^* - vd^* - \partial_t F_0 \Big|_{s^*=0} + vd \Big|_{s^*=0}) + O(L^2) \end{aligned}$$

for the other.

With (2.11), the two equations can be written in matching labels and just in terms of (α, t) :

$$L(\lambda_{\text{tether}} + \frac{1}{2}\lambda_{\text{area}})\nu = O(L^2) + \mu^A L(\partial_t F_0 - vd) + \mu^S \tilde{s} \frac{\partial a^*}{\partial s}(\alpha, 0) \left(v(d^*(a_0^*) - d) - \frac{\partial a}{\partial t}(a_0^*, 0) \partial_\alpha F_0 \right) \quad (2.18a)$$

$$L(\lambda_{\text{tether}}^*(a_0^*) + \frac{1}{2}\lambda_{\text{area}})\nu = O(L^2) + \mu^A L\left(\partial_t F_0 + \frac{\partial a}{\partial t}(a_0^*) \partial_\alpha F_0 - vd^*(a_0^*)\right) - \mu^S \tilde{s}^*(a_0^*) \frac{\partial a}{\partial s^*}(a_0^*, 0) \left(v(d - d^*(a_0^*)) + \frac{\partial a}{\partial t}(a_0^*, 0) \partial_\alpha F_0 \right). \quad (2.18b)$$

Multiplying (2.18b) by $\frac{\partial a^*}{\partial \alpha}(\alpha, 0)$ and adding it to (2.18a) cancels the interaction terms (like in Section 2.1), since

$$\lambda_{\text{tether}}(\alpha) + \frac{\partial a^*}{\partial \alpha}(\alpha, 0) \lambda_{\text{tether}}^*(a_0^*) = \lambda_{\text{tether}}(\alpha) - \frac{\partial a^*}{\partial \alpha}(\alpha, 0) \lambda_{\text{tether}}(\alpha) \frac{\partial a}{\partial \alpha^*}(a_0^*, 0) = 0$$

for the tether term and

$$\begin{aligned} \tilde{s} \left| \frac{\partial a^*}{\partial s} \right| &= \tilde{s}^* \left| \frac{\partial a}{\partial s^*} \right| \left| \frac{\partial a^*}{\partial \alpha} \right| \\ \int_{\tilde{s}}^0 \left| \frac{\partial a^*}{\partial s} \right| ds &= \int_{\tilde{s}^*}^0 \left| \frac{\partial a}{\partial s^*} \right| \left| \frac{\partial a^*}{\partial \alpha} \right| ds^* \\ \int_{\alpha^*: (\alpha, \alpha^*) \in \mathcal{C}} d\alpha^* &= \int_{\alpha: (\alpha, \alpha^*) \in \mathcal{C}} \left| \frac{\partial a^*}{\partial \alpha} \right| d\alpha, \end{aligned}$$

for the stretching term. It yields

$$\begin{aligned} \frac{L}{2} \left(1 + \frac{\partial a^*}{\partial \alpha}(\alpha, 0) \right) \lambda_{\text{area}} \nu &= \mu^A L \left(\partial_t F_0 \left(1 + \frac{\partial a^*}{\partial \alpha}(\alpha, 0) \right) + \frac{\partial a^*}{\partial t}(\alpha, 0) \partial_\alpha F_0 \right. \\ &\quad \left. - v \left(d + \frac{\partial a^*}{\partial \alpha}(\alpha, 0) d^*(a_0^*) \right) \right) + O(L^2). \end{aligned}$$

Dividing by L and passing to the limit $L \rightarrow 0$, we have

$$\begin{aligned} \frac{1}{2} \left(1 + \frac{\partial a^*}{\partial \alpha}(\alpha, 0) \right) \lambda_{\text{area}} \nu &= \mu^A \left(\partial_t F_0 \left(1 + \frac{\partial a^*}{\partial \alpha}(\alpha, 0) \right) + \frac{\partial a^*}{\partial t}(\alpha, 0) \partial_\alpha F_0 \right. \\ &\quad \left. - v \left(d + \frac{\partial a^*}{\partial \alpha}(\alpha, 0) d^*(a_0^*) \right) \right), \quad (2.19) \end{aligned}$$

which, considering $\omega^* = \omega + \varphi_0$ (2.13), results in a **transport equation for F_0** :

$$\begin{aligned} \partial_t F_0(\alpha, t) + \left(1 + \frac{\partial a^*}{\partial \alpha}(\alpha, 0, t) \right)^{-1} \frac{\partial a^*}{\partial t}(\alpha, 0, t) \partial_\alpha F_0(\alpha, t) &= \frac{\lambda_{\text{area}}(t)}{2\mu^A} \nu(\alpha, t) \\ + \left(1 + \frac{\partial a^*}{\partial \alpha}(\alpha, 0, t) \right)^{-1} v \left(d(\omega(\alpha, t)) + \frac{\partial a^*}{\partial \alpha}(\alpha, 0, t) d(\omega(\alpha, t) + \varphi_0) \right). \quad (2.20) \end{aligned}$$

Note that $1 + \frac{\partial a^*}{\partial \alpha}(\alpha, 0, t) > 0$ is nonzero for all (α, t) due to convention (C).

From (2.19), one can also deduce an **equation for λ_{area}** . Scalar multiplication by $\partial_\alpha F_0^\perp$ and integration over all α gives

$$\lambda_{\text{area}}(t) = \frac{2\mu^A v}{\int_0^{2\pi} |\partial_\alpha F_0^\perp(\alpha, t)| d\alpha} \int_0^{2\pi} \left(1 + \frac{\partial a^*}{\partial \alpha}(\alpha, 0, t)\right)^{-1} \partial_\alpha F_0^\perp(\alpha, t) \cdot \left(d(\omega(\alpha, t)) + \frac{\partial a^*}{\partial \alpha}(\alpha, 0, t) d(\omega(\alpha, t) + \varphi_0)\right) d\alpha. \quad (2.21)$$

The constraint for the area (1.12) was used and the fact, that the area of the cell stays constant in time: $\partial_t A_0 = 0$.

Furthermore, subtracting (2.18b) from (2.18a), dividing by L and passing to the limit $L \rightarrow 0$ yields

$$\lambda_{\text{tether}} \left(1 + \frac{\partial a}{\partial \alpha^*}(a_0^*, 0)\right) \nu = \left(\mu^A + \mu^S \left(M \frac{\partial a^*}{\partial s}(\alpha, 0) - M^* \frac{\partial a}{\partial s^*}(a_0^*, 0)\right)\right) \left(v(d^*(a_0^*) - d) - \frac{\partial a}{\partial t}(a_0^*) \partial_\alpha F_0\right).$$

Taking the normal component, i.e. scalar multiplying by ν , gives

$$\lambda_{\text{tether}} \left(1 + \frac{\partial a}{\partial \alpha^*}(a_0^*, 0)\right) = \left(\mu^A + \mu^S \left(M \frac{\partial a^*}{\partial s}(\alpha, 0) - M^* \frac{\partial a}{\partial s^*}(a_0^*, 0)\right)\right) v(d^*(a_0^*) - d) \cdot \nu,$$

which can be reorganized to an **equation for λ_{tether}** :

$$\lambda_{\text{tether}}(\alpha, t) = \left(1 + \left(\frac{\partial a^*}{\partial \alpha}(\alpha, 0, t)\right)^{-1}\right)^{-1} \left(\mu^A + \mu^S \left(M(\alpha, t) \frac{\partial a^*}{\partial s}(\alpha, 0, t) - M^*(\alpha, t) \frac{\partial a}{\partial s^*}(a_0^*, 0, t)\right)\right) v(d(\omega(\alpha, t) + \varphi_0) - d(\omega(\alpha, t))) \cdot \nu(\alpha, t). \quad (2.22)$$

On the other hand, taking the tangential component, i.e. scalar multiplying by $\partial_\alpha F_0$, gives

$$0 = \left(\mu^A + \mu^S \left(M \frac{\partial a^*}{\partial s}(\alpha, 0) - M^* \frac{\partial a}{\partial s^*}(a_0^*, 0)\right)\right) \left(v(d_0^* - d) \cdot \partial_\alpha F_0 - \frac{\partial a}{\partial t}(a_0^*) |\partial_\alpha F_0|^2\right),$$

which yields an evolution equation for the function $a(\cdot, 0, \cdot)$:

$$\frac{\partial a}{\partial t}(a^*(\alpha, 0, t), 0, t) = \frac{v}{|\partial_\alpha F_0(\alpha, t)|^2} (d(\omega(\alpha, t) + \varphi_0) - d(\omega(\alpha, t))) \cdot \partial_\alpha F_0(\alpha, t). \quad (2.23)$$

Multiplying this by $\frac{\partial a^*}{\partial \alpha}(\alpha, 0, t)$, we obtain a **transport equation for $a^*(\cdot, 0, \cdot)$** :

$$\frac{\partial a^*}{\partial t}(\alpha, 0, t) - \frac{v}{|\partial_\alpha F_0(\alpha, t)|^2} (d(\omega(\alpha, t) + \varphi_0) - d(\omega(\alpha, t))) \cdot \partial_\alpha F_0(\alpha, t) \frac{\partial a^*}{\partial \alpha}(\alpha, 0, t) = 0. \quad (2.24)$$

2.3 Discussion

To summarize, we gather the equations for the five true unknowns of the model:

(2.9) – Equation for the position F_0^* :

$$F_0^* \Big|_{s=0} = F_0$$

i.e. the centers of masses of two crossing filaments lie on the leading edge and coincide.

(2.20) – Equation for the position F_0 :

$$\begin{aligned} \partial_t F_0 + \left(1 + \frac{\partial a^*}{\partial \alpha} \Big|_{s=0}\right)^{-1} \frac{\partial a^*}{\partial t} \Big|_{s=0} \partial_\alpha F_0 \\ = \left(1 + \frac{\partial a^*}{\partial \alpha} \Big|_{s=0}\right)^{-1} v \left(d(\omega) + \frac{\partial a^*}{\partial \alpha} \Big|_{s=0} d(\omega + \varphi_0)\right) - \frac{\lambda_{\text{area}}}{2\mu^A} \frac{\partial_\alpha F_0^\perp}{|\partial_\alpha F_0^\perp|} \end{aligned}$$

The velocity is given by the lateral flow in tangential direction. Polymerization at the leading edge acts as a source and the limiting factor is the pressure arising from the area constraint. Note that λ_{area} is scaled like μ^A , so it cancels in the last summand and adhesion only contributes indirectly through the angle ω , see below.

(2.13) – Equation for the angle ω^* :

$$\omega^*(a^* \Big|_{s=0}) = \omega + \varphi_0$$

In the limit, the angle between two filaments of different families is in equilibrium.

(2.17) – Equation for the angle ω :

$$\begin{aligned} \left((\lambda_{\text{tether}} + \frac{1}{2}\lambda_{\text{area}}) d^\perp(\omega) + \Phi_0 \left(\frac{1}{2}\lambda_{\text{area}} - \lambda_{\text{tether}} \frac{\partial a^*}{\partial \alpha} \Big|_{s=0} \right) d^\perp(\omega + \varphi_0) \right) \cdot \frac{-\partial_\alpha F_0^\perp}{|\partial_\alpha F_0^\perp|} \\ = \mu^S \left[\frac{\partial a^*}{\partial s} \Big|_{s=0} (M^2 + M) d^\perp(\omega) \cdot \left((v(d(\omega + \varphi_0) - d(\omega)) \cdot \partial_\alpha F_0) \partial_\alpha F_0 \right. \right. \\ \left. \left. - v d(\omega + \varphi_0) \right) + \Phi_0 \frac{\partial a}{\partial s^*} (a^* \Big|_{s=0}, 0) (M^{*2} + M^*) d^\perp(\omega + \varphi_0) \right. \\ \left. \cdot \left((v(d(\omega + \varphi_0) - d(\omega)) \cdot \partial_\alpha F_0) \partial_\alpha F_0 + v d(\omega) \right) \right] \end{aligned}$$

The only contribution of adhesion to the model is through this equation for the angle, because only here μ^A appears inside the definition of λ_{area} .

(2.24) – Equation for the relating function a^* :

$$\frac{\partial a^*}{\partial t} \Big|_{s=0} - \frac{v}{|\partial_\alpha F_0|^2} (d(\omega + \varphi_0) - d(\omega)) \cdot \partial_\alpha F_0 \frac{\partial a^*}{\partial \alpha} \Big|_{s=0} = 0$$

This convection equation with velocity $-\partial_t a$ describes the lateral flow on the membrane. The difference of the directions multiplied by v gives the forward speed in

parameter space due to polymerization. The scalar product with the tangential vector projects it onto the membrane.

The rest are just complimentary equations:

$$(2.14) \quad \text{Equation for the weight } \Phi_0$$

$$(2.21) \quad \text{Equation for the Lagrange multiplier } \lambda_{\text{area}}$$

$$(2.22) \quad \text{Equation for the Lagrange multiplier } \lambda_{\text{tether}}$$

$$(2.12) \quad \text{Equation for the densities } \frac{\partial a^*}{\partial s} \text{ and } \frac{\partial a}{\partial s^*}$$

$$(2.15) \quad \text{Equation for the normalized integration bounds } M \text{ and } M_0^*.$$

Since we can calculate the position and the angle of the filaments of the *-family from the position and angle of the non-*-family, we can reduce the system to just three unknowns F_0, ω, a^* .

Reflecting about the solvability, we first regard some special cases:

Case 1: $\varphi_0 = 0$. This simplification implies parallel filaments: $d(\omega + \varphi_0) = d(\omega)$, which yields

$$\partial_t a^*(\alpha, 0, t) = 0$$

$$\lambda_{\text{tether}}(\alpha, t) = 0$$

$$\lambda_{\text{area}}(t) = 2\mu^A v \frac{\int_0^{2\pi} \partial_\alpha F_0^\perp \cdot d(\omega) d\alpha}{\int_0^{2\pi} |\partial_\alpha F_0^\perp| d\alpha} =: 2\mu^A v B.$$

The quotient B of the integrals represents the length of the mean normal component of the filament directions, since the denominator is the length of the leading edge.

The angle ω is given by

$$\frac{1}{2} \lambda_{\text{area}} (1 + \Phi_0) d^\perp(\omega) \cdot \nu = 0$$

which, for nonzero λ_{area} , is equivalent to

$$0 = d^\perp(\omega) \cdot \nu, \tag{2.25}$$

i.e. the filaments are orthogonal to the membrane, as expected. Since this means that $d = \nu$, the quotient B reduces to $B = -1$ and therefore

$$\partial_t F_0 = v d(\omega) (1 + B) = 0.$$

So we end up with a stationary system where only the angle has to be determined by the scalar equation (2.25), which expands to

$$0 = \partial_\alpha F_{0,1}(\alpha, 0) \cos \omega(\alpha, t) + \partial_\alpha F_{0,2}(\alpha, 0) \sin \omega(\alpha, t). \tag{2.26}$$

Case 2: $v = 0$. Also in the case of missing polymerization, there is no movement. We have

$$\begin{aligned}\partial_t a^*(\alpha, 0, t) &= 0 \\ \lambda_{\text{tether}}(\alpha, t) &= 0 \\ \lambda_{\text{area}}(t) &= 0,\end{aligned}$$

so the equation for F_0 reduces to

$$\partial_t F_0 = 0.$$

Division of the equation (2.17) for the angle ω by $v \neq 0$ makes it independent of v , so it remains valid for $v = 0$:

$$\begin{aligned}& \left((\lambda_T + \frac{1}{2}\lambda_A) d^\perp(\omega) + \Phi_0 \left(\frac{1}{2}\lambda_A - \lambda_T \frac{\partial a^*}{\partial \alpha} \Big|_{s=0} \right) d^\perp(\omega + \varphi_0) \right) \cdot \frac{-\partial_\alpha F_0^\perp}{|\partial_\alpha F_0^\perp|} \\ &= \mu^S \left[\frac{\partial a^*}{\partial s} \Big|_{s=0} (M^2 + M) d^\perp(\omega) \cdot \left(((d(\omega + \varphi_0) - d(\omega)) \cdot \partial_\alpha F_0) \partial_\alpha F_0 \right. \right. \\ &\quad \left. \left. - d(\omega + \varphi_0) \right) + \Phi_0 \frac{\partial a}{\partial s^*} (a^* \Big|_{s=0}, 0) (M^{*2} + M^*) d^\perp(\omega + \varphi_0) \right. \\ &\quad \left. \cdot \left(((d(\omega + \varphi_0) - d(\omega)) \cdot \partial_\alpha F_0) \partial_\alpha F_0 + d(\omega) \right) \right],\end{aligned}\tag{2.27}$$

where

$$\begin{aligned}\lambda_T := \frac{\lambda_{\text{tether}}}{v} &= \left(1 + \left(\frac{\partial a^*}{\partial \alpha}(\alpha, 0) \right)^{-1} \right)^{-1} \left(\mu^A + \mu^S \left(M \frac{\partial a^*}{\partial s}(\alpha, 0) \right. \right. \\ &\quad \left. \left. - M^* \frac{\partial a}{\partial s^*}(a_0^*, 0) \right) (d(\omega + \varphi_0) - d(\omega)) \right) \cdot \nu\end{aligned}$$

and

$$\begin{aligned}\lambda_A := \frac{\lambda_{\text{area}}}{v} &= \frac{2\mu^A}{\int_0^{2\pi} |\partial_\alpha F_0^\perp| d\alpha} \int_0^{2\pi} \left(1 + \frac{\partial a^*}{\partial \alpha}(\alpha, 0) \right)^{-1} \partial_\alpha F_0^\perp \\ &\quad \cdot \left(d(\omega) + \frac{\partial a^*}{\partial \alpha}(\alpha, 0) d(\omega + \varphi_0) \right) d\alpha.\end{aligned}$$

So we again have only one scalar equation to solve for ω , using that a^* and F_0 are given by the initial values of the functions:

$$\begin{aligned}a^*(\alpha, 0, t) &= a^*(\alpha, 0, 0) & \forall \alpha \\ F_0(\alpha, t) &= F_0(\alpha, 0) & \forall \alpha.\end{aligned}$$

Case 3: $\mu^A = 0$. In view of the motivational experiments, we also regard the case of no adhesion. Since the equations for F_0 and a^* are independent of μ^A , they remain

valid:

$$\frac{\partial a^*}{\partial t} \Big|_{s=0} - \frac{v}{|\partial_\alpha F_0|^2} (d(\omega + \varphi_0) - d(\omega)) \cdot \partial_\alpha F_0 \frac{\partial a^*}{\partial \alpha} \Big|_{s=0} = 0 \quad (2.28a)$$

and

$$\begin{aligned} \partial_t F_0 + \left(1 + \frac{\partial a^*}{\partial \alpha} \Big|_{s=0}\right)^{-1} \frac{\partial a^*}{\partial t} \Big|_{s=0} \partial_\alpha F_0 \\ - \left(1 + \frac{\partial a^*}{\partial \alpha} \Big|_{s=0}\right)^{-1} v \left(d(\omega) + \frac{\partial a^*}{\partial \alpha} \Big|_{s=0} d(\omega + \varphi_0) \right) + \lambda_A \frac{\partial_\alpha F_0^\perp}{|\partial_\alpha F_0^\perp|} = 0 \end{aligned} \quad (2.28b)$$

with

$$\begin{aligned} \lambda_A := \frac{\lambda_{\text{area}}}{2\mu^A} = \frac{v}{\int_0^{2\pi} |\partial_\alpha F_0^\perp(\alpha, t)| d\alpha} \int_0^{2\pi} \left(1 + \frac{\partial a^*}{\partial \alpha}(\alpha, 0, t)\right)^{-1} \partial_\alpha F_0^\perp(\alpha, t) \\ \cdot \left(d(\omega(\alpha, t)) + \frac{\partial a^*}{\partial \alpha}(\alpha, 0, t) d(\omega(\alpha, t) + \varphi_0) \right) d\alpha. \end{aligned}$$

With $\mu^A = 0$, we get

$$\lambda_{\text{area}} = 0,$$

so the equation for the angle reduces to

$$\begin{aligned} \lambda_{\text{tether}} \left(d^\perp(\omega) - \Phi_0 \frac{\partial a}{\partial \alpha^*} d^\perp(\omega + \varphi_0) \right) \cdot \frac{-\partial_\alpha F_0^\perp}{|\partial_\alpha F_0^\perp|} \\ = \mu^S \left[\frac{\partial a^*}{\partial s} \Big|_{s=0} (M^2 + M) d^\perp(\omega) \cdot \left((v(d(\omega + \varphi_0) - d(\omega)) \cdot \partial_\alpha F_0) \partial_\alpha F_0 \right. \right. \\ \left. \left. - v d(\omega + \varphi_0) \right) + \Phi_0 \frac{\partial a}{\partial s^*} (a^* \Big|_{s=0}, 0) (M^{*2} + M^*) d^\perp(\omega + \varphi_0) \right. \\ \left. \cdot \left((v(d(\omega + \varphi_0) - d(\omega)) \cdot \partial_\alpha F_0) \partial_\alpha F_0 + v d(\omega) \right) \right], \end{aligned} \quad (2.28c)$$

where

$$\lambda_{\text{tether}} = \left(1 + \left(\frac{\partial a^*}{\partial \alpha}(\alpha, 0)\right)^{-1}\right)^{-1} \mu^S \left(M \frac{\partial a^*}{\partial s}(\alpha, 0) - M^* \frac{\partial a}{\partial s^*}(a_0^*, 0) \right) v(d^* - d) \cdot \nu.$$

Here, the solvability is not as easy to see, which leads us back to the general case.

General case: When writing $u = (F_0, a^*) \in \mathbb{R}^3$, the system (2.20, 2.17, 2.24) has the following form:

$$\partial_t u + g(\omega, \partial_\alpha u) = 0 \quad (2.29a)$$

$$h(\omega, \partial_\alpha u) = 0 \quad (2.29b)$$

with initial conditions and periodic boundary conditions.

Taking the derivative of (2.29a) with respect to α and denoting $\partial_\alpha u =: v$, we get

$$\partial_t v + \partial_\alpha g(\omega, v) = 0. \quad (2.30)$$

If (2.29b) is solvable for ω , i.e. $\omega = H(v)$ for some function H , this can be plugged into (2.30):

$$\partial_t v + \partial_\alpha \underbrace{g(H(v), v)}_{=: f(v)} = 0. \quad (2.31)$$

This is a nonlinear conservation equation. A solution exists if it is hyperbolic, i.e. if and only if the Jacobian of the flux $f'(v)$ is diagonalizable and all its eigenvalues are real. The solution u to system (2.29) can then be obtained as the antiderivative of v .

Conclusion and Perspectives

Considering rigid filaments, the two phase FBLM was transformed into four integral equations and an ansatz for the filament position F was made. To be able to carry out the integration, the integration domain for the interaction terms was determined under the assumption of short filaments. For fixed label α , that filament of the $*$ -family was taken, which crosses it in $s = 0$. Expanding the functions depending on s around zero made it possible to integrate explicitly. Two special cases of the resulting system were regarded: The case of parallel filaments and the case of no polymerization. In these simplifications, no movement takes place. The question of solvability of the system in the general case remains open.

Possible modifications of the model could include individual filament lengths or different polymerization speeds. Also branching, capping and severing processes could be included.

Future work should deal with numerical simulations. As we have no theoretical conclusions about the solutions, the numerics would enable us to get some information. It needs to be checked, if simulations yield the same results as the complete FBLM, which would be a good indicator, that our formal limiting process is actually reasonable. It is to be expected, that these simulations will run with lower computational costs. If it is less costly to model a single cell, then it will become easier, for instance, to analyze multicellular systems. This simplified model could also be a good starting point to approach the current research objective, to let go of the traditional 2D studies and to simulate the behaviour of cells in a more realistic 3D setting. Recent experiments at the IST Austria suggest, that the requirement of adhesion could be overemphasized, as leukocytes with removed adhesion molecules still show movement under certain topologies of the tissue. Another idea is to derive a 3D model for the whole cell cortex analogously to the work in this thesis.

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Appendix: Derivation of $\lambda_{\text{tether}}^*$

The Lagrange multiplier corresponding to the condition, that all filaments share the leading edge, in this thesis is denoted by λ_{tether} . In [OS10a] it is denoted by λ_{edge} . It was first introduced on p.13, point (7), therein. The definition for the second family, however, turned out to be erroneous. It is missing the inner derivative arising from the chain rule in the calculation of the variation. It should read

$$\lambda_{\text{edge}}^-(t, \alpha) = -\frac{\partial \alpha^+}{\partial \alpha}(t, \alpha) \lambda_{\text{edge}}(t, \alpha^+(t, \alpha, 0)) \quad (\text{A.1})$$

instead. In our notation this corresponds to

$$\lambda_{\text{tether}}^*(\alpha^*, t) = -\frac{\partial a}{\partial \alpha^*}(\alpha^*, t) \lambda_{\text{tether}}(a(\alpha^*, 0, t), t) \quad (\text{A.2})$$

as used in (1.9).

Detailed derivation

We are using the notation of this thesis. The deviation between the outer edges of both filament families is described by the energy functional

$$U[F, F^*] = \int_{-\pi}^{\pi} \lambda_{\text{tether}}(\alpha, t) \left(F(\alpha, 0, t) - F^*(\hat{a}(\alpha, t), 0, t) \right) \cdot \nu(\alpha, t) d\alpha,$$

where $\hat{a}(\alpha, t)$ is chosen such that $F(\alpha, 0, t) - F^*(\hat{a}(\alpha, t), 0, t)$ is parallel to the outward unit normal vector $\nu(\alpha, t)$.

Splitting the integral into two and performing a change of variables $\hat{a}(\alpha, t) = \alpha^*$ in the second term yields

$$\begin{aligned} U[F, F^*] &= \int_0^{2\pi} \lambda_{\text{tether}}(\alpha, t) F(\alpha, 0, t) \cdot \nu(\alpha, t) d\alpha \\ &\quad - \int_0^{2\pi} \lambda_{\text{tether}}(\hat{a}^{-1}(\alpha^*, t), t) F^*(\alpha^*, 0, t) \cdot \nu(\hat{a}^{-1}(\alpha^*, t), t) \frac{\partial \hat{a}^{-1}}{\partial \alpha^*}(\alpha^*, t) d\alpha^*. \end{aligned}$$

Computing the variation of U in δF and δF^* respectively gives

$$\begin{aligned} \delta U[F, F^*] \delta F &= \frac{d}{d\varepsilon} \Big|_{\varepsilon=0} U[F + \varepsilon \delta F, F^*] \\ &= \int_0^{2\pi} \lambda_{\text{tether}}(\alpha, t) \delta F(\alpha, 0, t) \cdot \nu(\alpha, t) d\alpha \end{aligned}$$

and

$$\begin{aligned}\delta U[F, F^*] \delta F^* &= \left. \frac{d}{d\varepsilon} \right|_{\varepsilon=0} U[F, F^* + \varepsilon \delta F^*] \\ &= - \int_0^{2\pi} \lambda_{\text{tether}}(\hat{a}^{-1}(\alpha^*, t), t) \frac{\partial \hat{a}^{-1}}{\partial \alpha^*}(\alpha^*, t) \delta F^*(\alpha^*, 0, t) \cdot \nu(\hat{a}^{-1}(\alpha^*, t), t) d\alpha^*.\end{aligned}$$

Once the outer edges of the two families coincide, $\hat{a}^{-1}(\alpha^*, t)$ can be replaced by $a(\alpha^*, 0, t)$. Therefore, we have the Lagrange multipliers

$$\lambda_{\text{tether}}(\alpha, t) \quad \text{and} \quad \lambda_{\text{tether}}^*(\alpha^*, t) = -\lambda_{\text{tether}}(a(\alpha^*, 0, t), t) \frac{\partial a}{\partial \alpha^*}(\alpha^*, 0, t).$$