On Surface Growth of Actin Networks

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Dedicated to Professor Kumbakonam R. Rajagopal on the occasion of his 60th birthday

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Abstract

A continuum theory of surface growth is applied to the mechanical modeling of cell motility. The theory relies on a decomposition of the motion into deformation- and growth-inducing parts. A non-dissipative constitutive relation is adopted and expressed exclusively in terms of the current configuration. The resulting model is used in the simulation of a network of actin filaments, and a simple one-dimensional example is included to showcase its predictive capacity.

Keywords: Surface growth; non-dissipative material; continuum mechanics; actin networks.

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1 Introduction

Cell motility is an essential element of numerous physiological processes in multi-cellular organisms, including wound healing, embryonic development, and cancer metastasis. Motility in most cells can be classified as either crawling or swimming [1]. Crawling cells typically exhibit distinct protrusions from the body of the cell called pseudopodia. There is significant variety in the form of pseudopodia, including bulbous types, long finger-like extensions, and thin flat sheets [1]. A particular class of pseudopodia, referred to as lamellipodia, are known to be associated with directional motility in multiple cell types. One of the major mechanisms regulating the behavior of a lamellipodium during motility is the assembly and disassembly of actin filament networks (also known as the actin cytoskeleton) [2]. The lamellipodium essentially deconstructs itself at one end and reconstructs itself at the opposite end in a process known as treadmilling. As a result, the cell experiences an apparent motion which is primarily due to continuous surface growth/ablation and only secondarily due to conventional deformation.

Generally speaking, the network of actin filaments that creates and controls the lamellipodium is quite complex. While much of the experimental work to date is narrowly focused on quantifying individual mechanical properties of actin networks, a general picture of the constitutive behavior is beginning to emerge. Gardel et al. [3] report different elastic regimes in actin networks as a function of actin density. Similarly, Wachsstock et al. [4] note changes in the overall character (elastic, viscoelastic, viscous fluid) of actin networks as a function of cross-link types and reaction rates of cross-link proteins. Significant increases in stiffness for increasing strain rate in the presence of particular cross-link proteins are reported by Sato et al. [5]. The recent review by Stricker et al. [6] presents a summary of the current state of knowledge on the mechanics of the actin cytoskeleton. This includes a discussion of the dependence of the elastic properties on stress (or strain) and on the concentration of particular cross-linking and motor proteins, as well as of the ability of the network to self-regulate its stiffness at different rates of strain.

A continuum theory of surface growth is a natural setting for the modeling of actin network treadmilling in motile cells. To date, surface growth has received little attention in the continuum mechanics literature in comparison to volumetric growth, see [7, 8] for two recent theoretical contributions. The purpose of the present work is to apply the continuum theory of surface growth proposed by Hodge and Papadopoulos [9] to the problem of cell motility due to actin network treadmilling. This theory employs a decomposition of the
motion into deformation- and growth-inducing parts, and tracks material points relative to an evolving reference configuration, which reflects the fact that the set of material points in the body is changing continuously with time. The stress response is assumed non-dissipative and adheres to the general Eulerian constitutive framework proposed by Rajagopal and Srinivasa [10]. This is especially convenient since, due to surface growth, no single reference configuration can be used to determine the stresses at all times from a Lagrangian constitutive law.

The paper is organized in three major sections: Section 2 presents a review of the theory of surface growth. This is followed by the development of an implicit model of non-dissipative materials in Section 3. Finally, Section 4 includes the formulation of a one-dimensional initial/boundary-value problem of surface growth and documents its application to a simple actin cytoskeleton system.

2 A Theory of Surface Growth

2.1 Kinematics

One of the basic tenets of conventional continuum mechanics is that the set of material particles in a body remains fixed during the time of analysis. In this case, the material particles can be mapped bijectively to the region occupied by the body in the Euclidean point space at any given time. The invertibility of these configuration maps can be exploited to construct maps directly between any two configurations, thus obviating the need to directly involve the particles themselves in any kinematic considerations. In addition, the configuration at any given (and fixed) time may be chosen as the “reference” configuration, relative to which one may track deformation of the body.

In modeling physical processes such as surface growth, where material is added to or removed from the current surface of the body, it is clear that the construction of bijective maps between configurations poses a challenge. As advocated in [9], one option to address this challenge is to assume that a map between two configurations can be expressed as the composition of a purely material map (where the set of material particles is fixed) and a non-material surface growth map which tracks the evolution of the body’s surface due to growth. To this end, define the deformation map $\chi_d : \mathcal{R}^T \times \mathbb{R} \rightarrow \tilde{\mathcal{R}}^{\tau+t}$ on the configuration of the body at a given time $\tau$ as

$$\hat{x} = \chi_d(X, t; \tau) = \chi^\tau_d(X, t) ,$$

(1)
where the configuration $\mathcal{R}^\tau$ is assumed open and $\tilde{\mathcal{R}}^{\tau+t}$ is an intermediate configuration obtained by letting the body deform in the time interval $[\tau, t]$ without any growth. The notational convention adopted in (1), as well as in the remainder of the paper, is intended to emphasize that the variable(s) to the left of the semicolon may only be defined after the variable(s) to the right. Also, let the surface growth map $\chi_g : \partial\tilde{\mathcal{R}}^{\tau+t} \mapsto \mathcal{S}^{\tau+t}$ take the closed boundary $\partial\tilde{\mathcal{R}}^{\tau+t}$ on the intermediate configuration to its image $\mathcal{S}^{\tau+t}$ under growth at time $\tau + t$, which coincides with the boundary of the current configuration at time $\tau + t$. As a result, the position vector of any boundary point in the current configuration at time $\tau + t$ can be expressed as

$$\mathbf{x} = \chi_g(\tilde{\mathbf{x}}; \tau, t) = \chi^{\tau,t}_{\tau}(\tilde{\mathbf{x}}) ,$$

where $\tilde{\mathbf{x}}$ is on the boundary $\partial\tilde{\mathcal{R}}^{\tau+t}$. Note that a reference configuration is explicitly identified in (2) at time $\tau$. As $\tau$ increases, this configuration is updated to track the growth experienced by the body. The growth map $\chi^{\tau,t}_{\tau}$ is assumed to be a local diffeomorphism between the manifolds $\partial\tilde{\mathcal{R}}^{\tau+t}$ and $\mathcal{S}^{\tau+t}$. Once the boundary $\mathcal{S}^{\tau+t}$ is determined, the region $\mathcal{R}^{\tau+t}$ occupied by the body at time $\tau + t$ is defined by

$$\mathcal{R}^{\tau+t} = \text{int}(\mathcal{S}^{\tau+t}) ,$$

where “int” denotes the interior of an orientable surface. The regions $\tilde{\mathcal{R}}^{\tau+t}$ and $\mathcal{R}^{\tau+t}$ are schematically depicted in Figure 1.

The composition of the deformation and growth maps results in the apparent motion $\chi_a : \partial\mathcal{R}^\tau \times \mathbb{R} \mapsto \partial\mathcal{R}^{\tau+t}$ of points on the boundary $\partial\mathcal{R}^\tau$, which may be expressed as

$$\chi_a = \chi^{\tau,t}_{\tau} \circ \chi^\tau_d .$$

The decomposition (4) is an essential feature of the theory. Indeed, this decomposition enables the definition of the region $\mathcal{R}^{\tau+t}$ for bodies undergoing surface growth. As will be established later in this section, the decomposition (4) also permits a distinction between regions which contain material particles that existed at time $\tau$, and regions which contain material particles that came into existence after time $\tau$.

A mean rate of surface growth $\mathbf{v}_g$ relates points on the boundary $\partial\tilde{\mathcal{R}}^{\tau+t}$ of the intermediate configuration to points in the current configuration during the time interval $[\tau, \tau + t]$ as

$$\mathbf{v}_g = \frac{1}{t}(\mathbf{x} - \tilde{\mathbf{x}}) = \frac{1}{t}(\chi^{\tau,t}_{\tau}(\tilde{\mathbf{x}}) - \tilde{\mathbf{x}}) .$$
The normal component $v_g \cdot \mathbf{n}$ of this growth velocity quantifies the rate at which material is added ($v_g \cdot \mathbf{n} > 0$) or removed ($v_g \cdot \mathbf{n} < 0$) at the surface $\partial \tilde{R}^{\tau + t}$. No surface growth (or resorption) takes place when $v_g \cdot \mathbf{n} = 0$, where $\mathbf{n}$ denotes the outward unit normal to the surface $\partial \tilde{R}^{\tau + t}$. In such a case, the surface mass would change without any geometric change to the growth surface.

The preceding development depends crucially on the elapsed time $t$ between the reference and the current configuration. Certain restrictions need to be placed on the magnitude of $t$ on physical grounds. First, $t$ should be much smaller than the characteristic growth time $t_c$, defined as

$$t_c = \frac{L}{\|v_g\| \|\partial \tilde{R}^{\tau + t}\|}, \quad (6)$$

in terms of the $L_2$-norm $\|\cdot\|_{\partial \tilde{R}^{\tau + t}}$ of the growth velocity on $\partial \tilde{R}^{\tau + t}$ and an appropriately chosen characteristic measure of length $L$ for the reference configuration. This restriction ensures that some of the material particles in $\mathcal{R}^{\tau}$ survive in $\mathcal{R}^{\tau + t}$, thus ensuring that the deformation map $\chi_d$ is well-defined. Additionally, $t$ should be small enough so that it captures all desired growth events in the time interval $(\tau, \tau + t]$. This can be achieved by requiring that $v_g \cdot \mathbf{n}$ does not change sign between times $\tau$ and $\tau + t$ for any point on the boundary of the intermediate configuration corresponding to a material particle in the reference configuration. Further, $t$ should be small enough for the continuous interaction between deformation and surface growth to be satisfactorily represented in $(\tau, \tau + t]$ by the decomposition of the motion into the material and growth stages. A lower bound for $t$ is provided by requiring that the total linear growth in $(\tau, \tau + t]$ exceed the characteristic length of a typical molecular constituent of the growing material (e.g., the length of an actin monomer). Enforcement of this lower bound leads to the modeling of surface growth as a series of discrete growth “spurts” superposed on a deforming solid.

The foregoing kinematic development implies that the configuration $\mathcal{R}^{\tau + t}$ is comprised of material particles occupying two disjoint open sets in $E^3$: a material region $\mathcal{M}^{\tau + t}$ consisting of particles at $\tau + t$ that also existed at time $\tau$, and a growth region $\mathcal{G}^{\tau + t}$ with material particles that came to existence after time $\tau$. In addition, it is possible to define a surface $\sigma^{\tau + t}$, which corresponds to the interface between the material and growth regions, as

$$\sigma^{\tau + t} = \overline{\mathcal{M}^{\tau + t} \cap \mathcal{G}^{\tau + t}}. \quad (7)$$
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Now, the current configuration satisfies the condition

$$\mathcal{R}^{\tau+t} = \mathcal{M}^{\tau+t} \cup \mathcal{G}^{\tau+t} \cup \sigma^{\tau+t}.$$  \hspace{1cm} (8)

The ablated region $\mathcal{A}^{\tau+t}$ at time $\tau + t$ relative to time $\tau$ is also readily determined as

$$\mathcal{A}^{\tau+t} = \tilde{\mathcal{R}}^{\tau+t} \setminus \mathcal{R}^{\tau+t}.$$  \hspace{1cm} (9)

It is clear that the growth region $\mathcal{G}^{\tau+t}$ needs to be endowed with density, velocity and deformation information at time $\tau + t$. The existence of such extensions for various combinations of geometry and functional forms, as well as potential construction techniques, are discussed in [9].

2.2 Balance laws

A frame of reference is termed inertial if one may express Euler’s two laws relative to it in the canonical form

$$\dot{\mathbf{G}} = \mathbf{F}, \quad \dot{\mathbf{H}}^O = \mathbf{M}^O,$$  \hspace{1cm} (10)

as argued in Truesdell and Toupin [11, Sections 196-197]. Here, $\mathbf{G}$ is the linear momentum of the body (or any part of it), $\mathbf{F}$ is the resultant external force, $\mathbf{H}^O$ is the angular momentum about a fixed point $O$, and $\mathbf{M}^O$ is the resultant moment of the external forces about the point $O$. When using a non-inertial frame, extra terms are introduced into (10) as a result of the reformulation of the material time derivatives in terms of the non-inertial frame.

In this work, the frame of reference is assumed to move with frame velocity $\mathbf{v}_f (x, t; \tau)$ which does not coincide with the material velocity. The frame velocity is prescribed on the boundary $\partial \tilde{\mathcal{R}}^{\tau+t}$, such that

$$(\mathbf{v}_f - \mathbf{v}_d) \cdot \tilde{\mathbf{n}} = \mathbf{v}_g \cdot \tilde{\mathbf{n}}.$$  \hspace{1cm} (11)

This ensures that the non-inertial frame tracks the evolving boundary of the body, in the sense that the coordinates of this boundary remain fixed with respect to the moving frame. The extension of the frame velocity $\mathbf{v}_f$ to the interior $\tilde{\mathcal{R}}^{\tau+t}$ of the body is effected by appealing to a standard trace theorem, see [9]. No physical interpretation is assigned to $\mathbf{v}_f$ in the interior of the body, beyond the fact that it represents the velocity of a non-inertial frame attached to the growing boundary.
A global statement of balance of mass relative to the inertial frame can be readily derived by recalling the identity

$$\frac{d}{dt} \int_{\tilde{P}} \rho \, dv = \frac{\partial}{\partial t} \int_{\tilde{P}} \rho \, dv + \int_{\partial \tilde{P}} \rho \mathbf{v}_d \cdot \mathbf{n} \, da ,$$  \hspace{1cm} (12)

where $\frac{d}{dt}$ denotes the material time derivative, $\tilde{P} \subset \tilde{\mathcal{R}}^{r+t}$ is an arbitrary fixed region of the body with boundary $\partial \tilde{P}$, and $\rho$ is the mass density. Similarly, the balance of mass can be described relative to a non-inertial frame with frame velocity $\mathbf{v}_f$ as

$$\frac{d_f}{dt} \int_{\tilde{P}_f} \rho \, dv_f = \frac{\partial}{\partial t} \int_{\tilde{P}_f} \rho \, dv_f + \int_{\partial \tilde{P}_f} \rho \mathbf{v}_f \cdot \mathbf{n} \, da_f ,$$  \hspace{1cm} (13)

in an arbitrary fixed region $\tilde{P}_f \subset \tilde{\mathcal{R}}^{r+t}$ with boundary $\partial \tilde{P}_f$. Here, $\frac{d_f}{dt}$ denotes the time derivative keeping the coordinates of the non-inertial frame fixed. Recalling the identities in (12) and (13), setting $\tilde{P}_f = \tilde{P}$, and imposing conservation of mass in the material region $\tilde{P}$, leads to

$$\frac{d_f}{dt} \int_{\tilde{P}} \rho \, dv = \int_{\partial \tilde{P}} \rho (\mathbf{v}_f - \mathbf{v}_d) \cdot \mathbf{n} \, da ,$$  \hspace{1cm} (14)

which is the desired integral statement of mass balance. A local form may be deduced from (14) by using standard versions of the transport, divergence, and localization theorems, and reads

$$\frac{d_f}{dt} \rho + \rho \, \text{div} \mathbf{v}_d = \text{grad} \rho \cdot (\mathbf{v}_f - \mathbf{v}_d) .$$  \hspace{1cm} (15)

Statements of linear and angular momentum balance can be derived for the growing body by complete analogy to the derivation of mass balance. For linear momentum, the integral statement of balance takes the form

$$\frac{d_f}{dt} \int_{\tilde{P}} \rho \mathbf{v}_d \, dv = \int_{\tilde{P}} \rho \mathbf{b} \, dv + \int_{\partial \tilde{P}} \mathbf{t} \, da + \int_{\partial \tilde{P}} \rho \mathbf{v}_d [(\mathbf{v}_f - \mathbf{v}_d) \cdot \mathbf{n}] \, da ,$$  \hspace{1cm} (16)

where $\mathbf{b}$ is the body force per unit mass and $\mathbf{t}$ the surface traction on $\partial \tilde{P}$. The corresponding local form of linear momentum balance is

$$\rho \frac{d_f}{dt} \mathbf{v}_d = \rho \mathbf{b} + \text{div} \mathbf{T} + (\text{grad} \mathbf{v}_d) \rho (\mathbf{v}_f - \mathbf{v}_d) ,$$  \hspace{1cm} (17)

where $\mathbf{T}$ is the Cauchy stress tensor.
Angular momentum balance for the growing body can be expressed in the non-inertial frame as
\[
\frac{df}{dt} \int_P x \times \rho v \, dv = 
\int_P x \times \rho b \, dv + \int_P \left( e [T^T] + x \times \text{div} \, T \right) \, dv + \int_P \text{div} \left( (x \times \rho v_d) \otimes (v_f - v_d) \right) \, dv ,
\]
(18)
where \( e [\cdot] \) denotes the alternator tensor acting on a second-order tensor. Expanding the left-hand side of (18) and taking into account (15) and (17) leads to
\[
\int_P \frac{df}{dt} x \times \rho v_d \, dv = \int_P \left( e [T^T] + v_f \times \rho v_d \right) \, dv .
\]
(19)
Since \( \frac{df}{dt} = v_f \), balance of angular momentum yields the usual symmetry condition for the Cauchy stress tensor \( T \).

The preceding equations of motion may be viewed as a generalization of those obtained in the so-called Arbitrary Lagrangian-Eulerian formulation of conventional continuum mechanics, see [12] for a detailed exposition.

The Cauchy stress \( T \) is defined everywhere in the intermediate configuration at time \( \tau + t \), including the growth region that has come into existence by time \( \tau \) (i.e., the growth region that existed by the end of the previous time interval). In this region, the stress at time \( \tau + t \) may depend on the deformation gradient relative to the configuration at \( \tau \), as well as on other variables. An attractive alternative is to formulate the constitutive equations without explicit dependence on a reference configuration. This option is explored in the next section.

### 3 Stress Response of Non-Dissipative Actin Networks

The evolving nature of the reference configuration in the proposed theory of surface growth motivates the use of a constitutive law for the stress response which is independent of any reference configuration. The alternative would be to define stress at different material points as a function of the deformation relative to different reference states (as particles come to existence at various times), which is decidedly unappealing from a practical point of view. Since the current configuration at a given time is, in general, the only configuration shared by all particles in existence at that time, it is desirable to formulate the constitutive equations relative to this configuration.
Particular attention is focused here on the non-dissipative stress response of actin networks. Their macroscopic elastic deformation is due to microstructural stretching and rotations. There is also biological evidence that some non-dissipative processes contribute to the remodeling of the actin network. Indeed, it is thought that the dynamic behavior of both cross-linking and motor proteins may allow cells to tune the elastic behavior of actin networks in response to various loading conditions [6].

The non-dissipative stress response of actin networks is effected here using the constitutive framework proposed by Rajagopal and Srinivasa [10]. In particular, a Gibbs free energy is postulated as a function of the Cauchy stress \( \mathbf{T} \) and a non-singular Euleran anisotropic second-order tensor \( \mathbf{M} \), defined here as

\[
\mathbf{M} = \sum_{i=1}^{3} \mathbf{a}_i \otimes \mathbf{e}_i. 
\]

(20)

In (20), \( \mathbf{a}_i \) describe the geometry of microstructural features in the current configuration and \( \mathbf{e}_i \) are fixed orthonormal basis vectors, see [10]. Letting \( \overline{\mathbf{R}} (\overline{\mathbf{R}}^T \overline{\mathbf{R}} = \mathbf{I}) \) and \( \overline{\mathbf{U}} \) be the polar factors of \( \mathbf{M} \), the Gibbs free energy is assumed to take the form

\[
\Phi = \tilde{\Phi} (\mathbf{T}^*, \mathbf{K}) = \|\mathbf{T}^*\|^2 \alpha(\mathbf{T}^*, \mathbf{K}), 
\]

(21)

where \( \mathbf{T}^* = \overline{\mathbf{R}}^T \mathbf{T} \overline{\mathbf{R}} \) and \( \mathbf{K} = \overline{\mathbf{U}}^2 \). The functional form of \( \Phi \) in (21) is due to invariance, while the particular choice of \( \tilde{\Phi} \) ensures that the Gibbs free energy vanishes at zero stress. Recalling that the corresponding Helmholtz free energy per unit volume can be expressed as \( \Psi = \frac{\partial \Phi}{\partial \mathbf{T}^*} \cdot \mathbf{T}^* - \Phi \), it is shown in [10] that the condition

\[
\mathbf{D} = \overline{\mathbf{R}} \left\{ \frac{\partial^2 \Phi}{\partial \mathbf{T}^* \partial \mathbf{T}^*} [\mathbf{T}^*] + \frac{\partial^2 \Phi}{\partial \mathbf{T}^* \partial \mathbf{K}} [\mathbf{K}] - \mathbf{T}^* \left( \frac{\partial \alpha}{\partial \mathbf{K}} \cdot \mathbf{K} \right) \right\} \overline{\mathbf{R}}^T 
\]

(22)

is sufficient for non-dissipativeness (i.e., to enforce that \( \mathbf{T} \cdot \mathbf{D} - \dot{\Psi} = 0 \)). In equation (22), \( \mathbf{D} \) denotes the rate of deformation tensor.

Clearly, the particular form of \( \mathbf{a}_i \) depends on the material microstructure. The nature of \( \mathbf{a}_i \) is investigated here for the case of actin networks in motile cells. It is well-known that actin filaments organize into dendritic networks with the barbed ends pointed forward and with a characteristic angle of their major axes relative to the direction of travel [13]. Multiple interactions between two adjoining filaments are possible, including bulk deformation of the filament network, as well as rearrangement of individual filaments in the network. One possibility for the definition of the evolving microstructure of an actin network is shown in
Figure 2, which depicts the relation of the vector $\mathbf{a}_i$ to the different filament interactions. Specifically, the vector $\mathbf{a}_i$ is thought of as being attached at a point of one filament and at another point in the dendritic growth region emanating from this filament. Clearly, $\mathbf{a}_i$ will change by deformation of the two filaments and by reconfiguration (assumed here to be physically non-dissipative) of the new filament relative to the old. Given that the primary structural origin of dissipation in cells is an open question [14, 15], the assumption of non-dissipation of the actin network is tenable. Each of the two assumed processes affects the direction and magnitude of $\mathbf{a}_i$ and would generally induce changes in the stress.

A rate equation is stipulated for $\mathbf{a}_i$ in the form

$$\dot{\mathbf{a}}_i = \mathbf{G} \mathbf{a}_i,$$

where $\mathbf{G} = \tilde{\mathbf{G}}(\mathbf{L})$ is a tensor-valued function of the velocity gradient $\mathbf{L}$. In the special case where the vectors $\mathbf{a}_i$ evolve materially, it is trivial to see that $\tilde{\mathbf{G}}(\mathbf{L}) = \mathbf{L}$. Therefore, all deviations from microstructural materiality are captured by the constitutive function $\tilde{\mathbf{G}}$.

Invariance of the evolution equation (23) under superposed rigid motions necessitates that $\mathbf{G}$ transform according to

$$\mathbf{G}^+ = \mathbf{Q} \mathbf{G} \mathbf{Q}^T + \dot{\mathbf{Q}} \mathbf{Q}^T,$$

where $\mathbf{Q}$ denotes an arbitrary rotation on the current configuration.

In the following sections, the constitutive equations (22) and (23) are specialized to a simple one-dimensional actin model and are employed together with the requisite balance laws to demonstrate the behavior of a cellular body undergoing surface growth.

### 4 A One-dimensional Initial/Boundary-Value Problem

#### 4.1 Problem formulation

The strong form of the surface growth initial/boundary-value problem in one-dimension may be stated as follows: determine the density $\rho(\tilde{x}, t; \tau): \tilde{\mathbb{R}}^{\tau+t} \times I \mapsto \mathbb{R}$ and displacement $u(\tilde{x}, t; \tau): \tilde{\mathbb{R}}^{\tau+t} \times I \mapsto \mathbb{R}$ that satisfy the one-dimensional counterparts of (15) and (17), subject to the initial conditions

$$\rho(\tilde{x}, 0; \tau) = \rho_0(\tilde{X}) \text{ in } \mathbb{R}^\tau,$$

$$u(\tilde{x}, 0; \tau) = u_0(\tilde{X}) \text{ in } \mathbb{R}^\tau,$$

$$v_0(\tilde{X}) \text{ in } \mathbb{R}^\tau,$$

subject to the initial conditions

$$\rho(\tilde{x}, 0; \tau) = \rho_0(\tilde{X}) \text{ in } \mathbb{R}^\tau,$$

$$u(\tilde{x}, 0; \tau) = u_0(\tilde{X}) \text{ in } \mathbb{R}^\tau,$$

$$v_0(\tilde{X}) \text{ in } \mathbb{R}^\tau,$$
the boundary conditions
\[ u = \bar{u}(\tilde{x}, t; \tau) \text{ on } \tilde{\Gamma}_u \times \mathcal{I} , \]
\[ t = \bar{t}(\tilde{x}, t; \tau) \text{ on } \tilde{\Gamma}_q \times \mathcal{I} , \]
and the extensions of \( \rho, u, \) and \( v_d \) into the growth region \( G \) discussed later in Section 4.2.
In the above, \( X \) is the coordinate in the updated reference configuration at time \( \tau \) and \( \rho_0, u_0 \) and \( v_0 \) are initial conditions at \( \tau \) deduced by previously solving the problem in the domain \( (0, \tau] \). Also, \( \mathcal{I} \) is the time interval \( (\tau, \bar{T}] \), where \( \bar{T} \) is the terminal time of interest for the preceding initial/boundary-value problem. Finally, the domains of the Dirichlet and Neumann boundary conditions (26) satisfy \( \tilde{\Gamma}_u \cup \tilde{\Gamma}_q = \partial \tilde{\mathcal{R}}_{\tau+t} \). It is emphasized here that the frame velocity \( v_f \) is assumed to be known throughout the domain occupied by the body in its intermediate configuration.

In this one-dimensional case, the constitutive equation (22) reduces to
\[ D = \frac{\partial^2 \Phi}{\partial T^2} \tilde{T} + \frac{\partial^2 \Phi}{\partial T \partial K} \tilde{K} - T \frac{\partial \alpha}{\partial K} \tilde{K} . \]  
(27)
Here \( T \) and \( K \) are the scalar counterparts of the tensors \( \mathbf{T} \) and \( \mathbf{K} \). The latter is obtained from the reduced anisotropic tensor
\[ \mathbf{M} = a \otimes \mathbf{e}_1 = a \mathbf{e}_1 \otimes \mathbf{e}_1 , \]  
(28)
as \( K = a^2 \), where \( \mathbf{e}_1 \) is the unit vector along the direction of the body and \( a \) is the magnitude of \( a_1 \). The evolution of \( a \) is governed by the one-dimensional counterpart of (23) in the form
\[ \dot{a} = Ga , \]  
(29)
where \( G \) is a scalar-valued function of the velocity gradient \( L \). An initial condition of the form \( a(t = 0) = a_0 \) is necessary for the solution of the preceding equation. Upon substituting the assumed Gibbs free energy
\[ \Phi = T^2 \alpha(K) \]  
(30)
into (27) and taking into account the definition of \( K \), the constitutive equation is reduced to
\[ D = 2\alpha \tilde{T} + 2 \frac{\partial \alpha}{\partial K} KGT . \]  
(31)
When $D$ is specified, (31) becomes a first-order ordinary differential equation for the Cauchy stress $T$. Any standard discrete time integrator may be employed to approximate the solution of this equation. For instance, the implicit backward Euler method in the time interval $(t_n, t_{n+1}]$ yields

$$
T_{n+1} = \left( \tilde{C}_{n+1} + \Delta t_n \tilde{K}_{n+1} \right)^{-1} \left[ \Delta t_n D_{n+1} + \tilde{C}_{n+1} T_n \right],
$$

(32)

where $\tilde{C}_{n+1} = 2\alpha_{n+1}$, $\tilde{K}_{n+1} = 2 \frac{\partial \alpha}{\partial K} \bigg|_{n+1} K_{n+1} G_{n+1}$ and $\Delta t_n = t_{n+1} - t_n$. Also, $K_{n+1} = a_{n+1}^2$, where $a_{n+1}$ is determined from the discrete counterpart of (29) as

$$
a_{n+1} = (1 - \Delta t_n G_{n+1})^{-1} a_n.
$$

(33)

### 4.2 A one-dimensional example

The proposed formulation of surface growth, along with the constitutive equation (31) are used to explore the mechanical behavior of a one-dimensional idealization of an actin cytoskeleton experiencing both growth and deformation. Piecewise linear finite elements are employed in the solution of the weak (Galerkin) counterparts of (15) and (17). The constitutive equation is integrated in time according to (32) and (33), while time integration of the momentum balance equations is performed using the classical Newmark method. A Lagrange multiplier method is implemented to impose the geometric constraint of constant jump in the displacement at each growth interface point.

The cytoskeleton is assumed fixed on one end (where a no-growth condition is assumed) and free on the other with homogeneous Neumann boundary condition and specified growth velocity $v_g$. A uniform tension-inducing body force $b$ per unit mass is applied throughout the domain $\mathcal{R}^0$ of the cytoskeleton. The problem data are as follows:

$$
\begin{align*}
\mathcal{R}^0 &= (0, 10) \, \mu m, \\
\rho_0 &= 1 \times 10^{-9} \, mg/\mu m, \\
b &= 1.96 \times 10^{10} \, pN/mg, \\
v_g &= 5 \, \mu m/s, \\
a_0 &= 1 \, \mu m.
\end{align*}
$$

(34)

Two choices are considered for the scalar function $\alpha$ that enters the Gibbs free energy in (30). In the first case,

$$
\alpha = \alpha_0.
$$

(35)
where the value $\alpha_0 = 10^{-4} \mu m^2/pN$ is derived from experimental measurements for the Young’s modulus of actin [16]. In the second case,

$$\alpha = \alpha_1 K,$$

where $\alpha_1 = 10^{-4} 1/pN$. Note that, for visualization purposes, the values of the body force and the growth velocity are exaggerated relative to typical cell values.

The extension of relevant fields into the growth region, noted in Section 2.1, is effected as follows. The density is extended continuously across the point $\sigma^{\tau + t}$ and is initially constant in the growth region $G^{\tau + t}$. As the material in $G^{\tau + t}$ comes into existence, its deformation gradient is specified as $F = 1$; therefore, in general, the deformation gradient exhibits a finite jump across $\sigma^{\tau + t}$. As with the density, the extension of the velocity in $G^{\tau + t}$ is continuous across $\sigma^{\tau + t}$ and initially constant. The continuity of the velocity guarantees geometric compatibility between the material and the growth region. In addition, the initial value of the anisotropic parameter $a$ in $G^{\tau + t}$ is set to $a = 1$, consistently with its (initial) value in the material region. Finally, the initial stress in the growth region is specified as equal to zero, which generally does not satisfy momentum balance across $\sigma^{\tau + t}$. However, the immediately ensuing enforcement of the balance laws in the combined region restores the balance of momentum everywhere in the configuration of the body.

For the choice of $\alpha$ in (35), the constitutive equation reduces to a simple hypoelastic-like form

$$D = 2\alpha \dot{T} .$$

Figure 3 depicts the displacement field after 10 growth “spurts” (time $t = 1.0 s$). The displacement in the original material portion of the body shows the expected quadratic profile, while jumps exist in the growth region due to the addition of new material, whose displacement is tracked relative to the configuration at the time of its creation. Figure 4 shows the Cauchy stress distribution at time $t = 1.0 s$. As expected, the stress attains a maximum at the fixed end and decreases linearly to zero on the free end. Also, linear momentum balance enforces continuity of the stress.

In the second case, corresponding to $\alpha$ as in (36), the constitutive equation becomes

$$D = 2\alpha \dot{T} + 2\alpha G T .$$

Additionally, the coefficient $G$ in equation (29) is assumed to be

$$G = cL ,$$

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where $c$ is a constant, so that $c = 1$ corresponds to the material evolution of $a$. For any case other than $c = 1$, the evolution of $a$ is affected by both deformation and reconfiguration of the microstructure. The displacement of the actin cytoskeleton after 10 growth spurts is shown in Figure 5 for $c = 0.2$, 1.0, and 2.0. It is concluded that the stiffness of the body decreases with $c$, as readily anticipated from (38).

5 Conclusions

A model of surface growth is developed and applied to the actin cytoskeleton of lamellipodia. The model makes use of an non-dissipative constitutive law that does not depend on any reference configuration. This Eulerian formulation of the constitutive law simplifies the modeling task in light of the complexity associated with the evolving nature of the reference configuration due to growth/ablation. Different constitutive choices are explored within a simple one-dimensional setting using a finite element approximation. The discontinuous displacement field is determined from the solution of a representative initial/boundary-value problem, with each discontinuity corresponding to an earlier growth spurt.

References


Figure 1: A schematic depiction of typical configurations $\mathcal{R}_\tau$ (reference), $\tilde{\mathcal{R}}^{\tau+t}$ (intermediate) and $\mathcal{R}_\tau^{\tau+t}$ (current) in the theory of surface growth.
Figure 2: Interpretation of the behavior of one possible definition of the vector $\mathbf{a}$ for an actin fiber network.
Figure 3: Displacement versus position for $\alpha = \alpha_0$ after 10 growth spurts ($t = 1.0$ s).
Figure 4: Cauchy stress versus position after 10 growth spurts ($t = 1.0 \, s$).
Figure 5: Displacement versus position for $\alpha = \alpha_1 K$ after 10 growth spurts ($t = 1.0$ s) with $c = 0.2, 1.0$ and 2.0.