The cytoskeleton is an important cellular substructure involved in many vital processes like cell division, cell locomotion, and the organization of intracellular transport [1,2]. Its main constituents, actin and tubulin, form long filamentous polymer chains, called actin filaments and microtubules, respectively. At first sight, the cytoskeleton thus appears to be a physical gel. Two features of this filament network, however, clearly distinguish the cytoskeleton from typically studied physical gels. For one, the two ends of an actin filament or a microtubule are structurally different, implying a possible polar order of the gel. For the other, the cytoskeleton is intrinsically out of thermodynamic equilibrium which can, in particular, lead to self-organization of purified cytoskeletal components in vitro [3–5].

The cytoskeleton is maintained out of equilibrium by a constant flux of energy through the system, which is provided by the hydrolysis of adenosine triphosphate. It is used to drive a number of molecular processes, notably the action of molecular motors, which are proteins that can move directionally along filaments, but also the polymerization and depolymerization of filaments [1,2]. The combination of filament polarity and the active addition and removal of subunits can lead to treadmilling, such that subunits are removed at one filament end, called the minus end, and added at the other, the plus end. Treadmilling is essential for a number of cellular processes, in particular, the crawling of cells like fibroblasts or keratocytes on a substrate (both cell types play a role in wound healing) [6], and for the maintenance of important cellular structures, e.g., the stereocilia of hair cells, which are essential for hearing in vertebrates [7].

Physical aspects of cytoskeletal dynamics have been studied using macroscopic phenomenological theories, which emphasize the role of symmetries rather than specific molecular processes, see for example [8–10]. In this case, dynamic equations are obtained from a systematic expansion with respect to an appropriately chosen reference state. In the expansion only terms compatible with the system’s symmetries are kept. In contrast, more microscopic theories start at the level of molecular processes, see for example [11–14]. While phenomenological descriptions emphasize generic properties, the more microscopic theories can connect molecular processes to collective behavior.

The latter approach has so far been applied either to systems where the filaments can change their length, but where spatial degrees of freedom can be neglected [11]. Or, monodisperse systems were considered, where all filaments are of the same length and are transported due to the action of molecular motors [12–14]. However, combining these two aspects in one framework is necessary when aiming at a description of cellular structures and processes.

In this Letter, we present a microscopic framework for combining treadmilling and spatial degrees of freedom for the filaments. A direct analytical and even a numerical study of these equations is practically impossible, though. By introducing a hierarchy of order parameters, we obtain a form that is amenable for analysis. In a two-dimensional geometry, we find the system to self-organize into stationary asters or moving spots if proteins are present that

FIG. 1. Schematic representation of the different processes described by Eqs. (1)–(4). Subunits of length δ attach at rate $k_a$ to the plus-end (a) and detach at rate $k_d$ from the minus end (b). Regulating proteins are transported by molecular motors along filaments at velocity $v_n$ (c). Shown is the case of a protein promoting filament nucleation.
regulate filament nucleation and that are transported by motors; see Fig. 1. Respectively, these states are strongly reminiscent of structures formed in moving keratocyte fragments [15] and in melanophore fragments [16,17]. We finally discuss our results in the light of these cellular structures.

In our description, the state of the system is determined by the densities of filaments and of regulating proteins. Free monomers are assumed to form a reservoir such that they do not appear explicitly in our description. The filament distribution is described by the density of plus-ends \( c \), which depends on the position \( \mathbf{r} \), the filament orientation \( \mathbf{u} \), where \( \mathbf{u}^2 = 1 \), the filament length \( \ell \), and time \( t \). In particular, \( c(\ell = 0) \) describes the density of filaments of minimal length, i.e., nuclei [1,2]. We assume that the length of a filament can change by filament growth at the plus-end and by shrinkage at the minus end. The corresponding effective rates times the length added or removed by the densities of filaments and of regulating proteins.

\[ \rho_i(\mathbf{r}, t) = \int_0^\infty d\ell \int_0^\ell d\xi \nabla \cdot \mathbf{j}(\mathbf{r}) \]

where \( \mathbf{j}(\mathbf{r}) = -v_n \mathbf{n}(\mathbf{r}) \int_0^\infty d\ell \int_0^\ell d\xi \xi^{d-1} d\mathbf{u} \mathbf{c}(\mathbf{r} + \xi \mathbf{u}, \mathbf{u}, \ell) \]

(4)

where \( v_n \) is the average transport velocity of nucleators along filaments and \( d \) the dimension of space.

Equations (1)–(4) specify the dynamics of treadmilling filaments in the presence of nucleators. Because of the form of the current (4) and because \( c \) depends on five variables (if \( d = 2 \)), a direct analysis of these equations is hardly feasible. Therefore, we perform an expansion in moments of the orientation \( \mathbf{u} \) and the filament length \( \ell \), which leads to a hierarchy of order parameters defined by

\[ \rho_i(\mathbf{r}, t) = \int_0^\ell d\ell' \int_0^{\ell'} d\mathbf{u} c(\mathbf{r}, \mathbf{u}, \ell, t) \]

(5)

\[ \mathbf{p}_i(\mathbf{r}, t) = \int_0^\ell d\ell' \int_0^{\ell'} d\mathbf{u} \mathbf{c}(\mathbf{r}, \mathbf{u}, \ell, t) \]

(6)

where \( i = 0, 1, 2, \ldots \) and only the first two moments in \( \mathbf{u} \) are given. We will truncate this hierarchy to obtain a finite set of equations. The truncation can be performed at a low order, as long as one restricts attention to structures that vary hardly over the average filament length \( \rho_i/\rho_0 \).

Coarse graining the dynamic Eqs. (1)–(4), the time evolution of the order parameter fields reads in dimensionless form

\[ \partial_t \rho_i = \nabla^2 \rho_i - \bar{\nabla}_a \nabla \cdot \mathbf{p}_i + i(\bar{\nabla}_a - \bar{\nabla}_d) \delta_{i0} n - \rho_{i-1} \]

(7)

\[ \partial_t \mathbf{p}_i = \nabla^2 \mathbf{p}_i - \frac{\bar{\nabla}_d}{2} \mathbf{p}_i + i(\bar{\nabla}_a - \bar{\nabla}_d) \mathbf{p}_{i-1} - \mathbf{p}_i \]

(8)

\[ \partial_t n = \bar{\nabla}_d \nabla^2 n - \nabla \cdot \mathbf{j} \]

(9)

In this expression, \( \delta_{ij} \) is the Kronecker delta and we have rendered the densities dimensionless: \( \bar{\rho}_i = \rho_i \ell^{2-i} \), \( \bar{\mathbf{p}}_i = \mathbf{p}_i \ell^{2-i} \), and \( \bar{n} = n \ell^2 \) with \( \ell \equiv \sqrt{D/\nu_d} \) (for the fields the bars have been omitted in the above equations). The dimensionless parameters are \( \bar{\nabla}_a = v_a/\sqrt{D\nu_d} \), \( \bar{\nabla}_d = v_d/\sqrt{D\nu_d} \), \( \bar{\nu} = 2\pi \nu \ell \) and \( \bar{D}_n = D_n/\ell^2 \). Note, that Eqs. (7) and (8) are closed in moments, that is, the time evolution of \( \rho_i \) and \( \mathbf{p}_i \) only depend on \( \rho_j \) and \( \mathbf{p}_j \) with \( j \leq i \).

This holds whenever the parameters are independent of \( \ell \).

We will truncate the hierarchy at \( i = 4 \). We have checked in one spatial dimension by a direct comparison of solutions to the full dynamic equations and solutions for the truncated hierarchy, that the asymptotic dynamic states are correctly described by the truncated equations. In the following, we consider two spatial dimensions. The nucleator current then reads

\[ \mathbf{j} = \bar{\nu}_n \{ \mathbf{p}_2 + \frac{1}{2} \nabla \rho_3 + \frac{1}{16} \nabla \cdot \gamma_4 \} \]

(10)

with dimensionless nucleator velocity \( \bar{\nu}_n = v_n/\sqrt{3D\nu_d} \).

The tensor \( \gamma_4 \) has components.
\[
\gamma_{4,\alpha\beta} = \frac{\partial p_{4,\alpha}}{\partial x_{\beta}} + \frac{\partial p_{4,\beta}}{\partial x_{\alpha}} + \delta_{\alpha\beta} \nabla \cdot p_4 \tag{11}
\]

with \(\alpha, \beta = 1, 2\).

We analyze the system constituted by Eqs. (7)–(11) in two spatial dimensions and for an infinite domain size. The homogenous isotropic state \(n = n_0, \rho_0 = n_0 \bar{\rho} (\bar{u}_a - \bar{u}_f)\), \(\rho_i = i(\bar{u}_a - \bar{u}_f) \rho_{i-1}\), \(p_i = 0\) for \(i = 1, 2, 3, 4\) is a stationary state of the dynamic equations for all values of \(\bar{\rho}, \bar{D}_n\), and \(\bar{u}_a \approx \bar{u}_f\). In Fig. 2 we show the corresponding stability diagram as a function of \(\bar{u}_a\) and \(\bar{u}_f\). There are two stability boundaries, one for \(\bar{u}_n > 0\), one for \(\bar{u}_n < 0\). In the first case, the instability is always oscillatory, while in the second case, the instability is oscillatory for \(\bar{u}_n > 0\) larger than a critical value, but stationary otherwise. All bifurcations are subcritical. We will now more closely examine the states in the unstable region.

Consider the case \(\bar{u}_n > 0\), which corresponds to a transport of nucleators towards filament plus-ends. For values of \(\bar{u}_n\) larger than the critical values, the system self-organizes into a solitary wave, see Fig. 3. Remarkably, the state is topologically not a plane wave. Instead, it carries a singularity at the leading edge and the filament distribution is crescent shaped. The lines of the filament flow are essentially aligned with the polarization field, which is pointing away from the singularity.

Traveling wave solutions for \(\bar{u}_n < 0\) share many features with the one described in the previous paragraph. However, there is now a periodic pattern of moving crescent-shaped spots. An example is shown in the inset of Fig. 2. In these patterns, too, the distribution of nucleators is concentrated at the leading edge, even though the nucleator velocity is directed to the minus ends filaments. The nucleator current, however, is dominated by the term \(\nabla \rho_3\), such that it is directed opposite to the polarization.

We now turn to the stationary heterogeneous and anisotropic solutions of the dynamic equations, which occur for sufficiently small values of \(\bar{\rho}_n\), if \(\bar{\rho}_n\) exceeds a critical value. The system then organizes into asters which are circularly symmetric. The filament and nucleator densities are maximal in the aster’s center. The maxima coincide with a singularity of the polarization field. The polarization vector points into the radial direction away from the singularity.

The system will eventually always form a single aster. Initially, however, many small asters may be present. In the course of time, these asters will fuse and the pattern coarsens, see Fig. 4, insets. We investigated the coarsening in more detail by studying two interacting asters in the limiting case of vanishing nucleator diffusion, \(\bar{D}_n = 0\). In that case, the equations for the stationary state can be solved analytically by means of the Fourier-Bessel transform if one assumes rotational symmetry of the fields and that the polarization vector always points radially. Furthermore, the nucleator density is assumed to be given by a \(\delta\)-distribution at the center of each aster. We find solutions for all values of \(\bar{u}_n < 0\).

Since Eqs. (7)–(11) are linear in this case, the fusion of two asters can be studied by calculating the velocity of the \(\delta\)-peaked nucleator distribution of one aster in the filament density and polarization fields of the other aster. The result of such a calculation is presented in Fig. 4, main panel and shows very good agreement with the numerical solution to the full equations.

In this Letter, we have presented a formalism for describing the dynamics of treadmilling filaments in the presence of proteins affecting the addition and removal of filament subunits. The crucial step for analyzing the corresponding dynamic equations is to perform a moment expansion in terms of the filament length, which leads to a hierarchy of order parameters. The analysis of this system in an infinite geometry revealed the existence of asters and moving spot solutions to the dynamic equations.

FIG. 2. Stability diagram of the stationary homogenous isotropic state of Eqs. (7)–(11) as a function of the nucleator and the polymerization velocities, \(\bar{u}_a\) and \(\bar{u}_f\). The full lines indicate oscillatory, the dashed line stationary instabilities. Dots indicate back transitions. Insets illustrate emergent states in the nonlinear regime by their filament densities and polarization fields. Parameter values are \(\bar{u}_f = 3\), \(\bar{D}_n = 4\), \(\bar{\rho} = 2\pi\), and \(n_0 = 0.01\).

FIG. 3. Snapshot of a crescent-shaped solitary wave solution to Eqs. (7)–(11). Left: nucleator density, right: gray scale coded filament density \(\rho_0\) and polarization field \(p_0\). The wave moves to the left. The polarization field has a singularity at the rear end, the nucleators are predominantly localized at the leading edge of the filament spot. Parameter values are \(\bar{\rho}_n = 7\) and \(\bar{u}_n = 1\). Other values are as in Fig. 2. Periodic boundaries have been employed. The simulation domain size is \(20 \times 20\).
We can compare these solutions to cellular structures. Let us start with the moving spots. Many of their features are strongly reminiscent of moving keratocyte fragments [15]. They also assume a crescent shape and the actin filaments point predominantly towards the leading edge. In the case of keratocytes, the nucleating proteins are Wiskott-Aldrich syndrom proteins (WASP), which nucleate new branches of actin filaments by activating the Arp2/3 complex [6]. WASP is located at the leading edge of a moving fragment. The molecular details of the localization of WASP are not yet understood, but active transport along actin filaments is likely to be involved.

There are, however, a number of differences between the states observed here and real keratocyte fragments. The most obvious one is that fragments are finite objects enclosed by a membrane. Therefore, there is a maximal length of the fragments which depends on their position and their orientation. A possible way to treat this problem consists of describing the boundary by a potential and will be described elsewhere. Since the real system is finite, the filament subunits can no longer be treated as a reservoir. Hence, material needs to be transported and this end momentum needs to be exchanged with the environment. Momentum is exchanged by attachment of the filaments to the substrate, which we have not included in our description, but it can easily be done, see Ref. [18]. Furthermore, a retrograde flow of actin has been observed in fragments. This is not the case in the solutions observed here. Through an analysis of a phenomenological description of active polar gels, the retrograde flow has been attributed to active stresses generated in the actin gel [19]. So, the framework developed above should be combined with theories on systems where motors act as active cross-linkers [12–14].

We can also compare the aster solutions to patterns of microtubules and granules in fragments of fish melanophores [16,17]. In these systems, color granules agglomerate in the center of a melanophore fragment. This agglomeration is accompanied by a rearrangement of microtubules which form an aster. The granules are linked to motors and can nucleate new microtubules [20]. In agreement with our findings, it had been shown by modeling, that these features are sufficient for generating the observed structures [21,22].

In the future it will be interesting to apply the present framework in the study of effects of proteins other than nucleators on systems of treadmilling filaments and to compare them to in vivo structures.