C 7 Hydrodynamics of the active cytoskeleton

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1 Introduction

From a physical point of view, the spontaneous emergence of flows and topological point defects through the internal conversion of chemical energy are among the most exciting features of the cytoskeleton and of filament-motor systems in general [1, 2]. In contrast to conventionally studied polymer solutions, these phenomena are not due to the application of an external field, but result from processes within the material. Specifically, the free energy released in the process of Adenosine-Triphosphate (ATP) hydrolysis generates conformational changes of motor proteins and affects filament assembly. The resulting force dipoles produce an ”active stress”, which drives the aforementioned processes.

Various physical approaches have been pursued to describe cytoskeletal dynamics. The most detailed descriptions are agent-based stochastic processes that are usually studied numerically. A prominent example of this approach is given by the Cytosim package, which includes a broad variety of cytoskeletal elements [3]. To give but two examples, it has been used to study the self-organization of microtubules and kinesins into asters and vortices [1] and to investigate the conditions under which an actomyosin network contracts [4]. In addition, stochastic simulations are developed with the specific purpose to study a concrete phenomenon, for example, the emergence of actin polymerization waves [5] or cortical actin length distributions [6].

Kinetic descriptions can be seen as mean-field theories of the stochastic processes just mentioned. They are continuum descriptions, where the expressions for the currents and the reactions are motivated by known molecular processes. However, they typically neglect molecular details and focus on the (hopefully) essential aspects of the molecular interactions and dynamics. Such approaches have been used to study possible mechanisms of stress generation in filament-motor networks [7, 8], the possible role of actin-polymerization waves for cell migration [9], and pattern formation in contractile rings [10].

Finally, phenomenological descriptions for macroscopic cytoskeletal dynamics have been developed [11]. Non-equilibrium thermodynamics, which is also known as generalized hydrodynamics, provides a framework for the systematic derivation of the corresponding dynamic equations if the material is close to thermodynamic equilibrium [12, 13]. This condition is expressed by the requirement that the system is locally at equilibrium. Non-equilibrium thermodynamics is purely based on symmetries and conservation laws. The material properties are captured by constitutive equations that are obtained from a systematic expansion of the currents in terms of thermodynamic forces. The latter are in turn expressed in terms of the state variables, such that a closed set of equations is obtained. Notably, the active stress is written as a linear function of the difference between the chemical potentials of ATP and its hydrolysis products. Hydrodynamic equations depend on a number of phenomenological constants, for example, the viscosities of simple fluids. Their values either have to be measured or can be related to molecular parameters by using a kinetic or agent-based description.

The hydrodynamics of active gels – or active gel theory – has been used to study generic physical properties of the cytoskeleton, for example, the dynamics of topological point defects or the spontaneous emergence of flows [11, 14, 15]. In addition, it has been employed to analyse subcellular and tissue dynamics. For example, the retrograde flow in lamellipodia [16], the formation and contraction of cytokinetic rings during cell division [17], or the spreading of epithelia during embryonic development were analyzed in this framework [18].

In this chapter, we will sketch the ideas underlying general hydrodynamics and use it to derive the dynamic equations of an active gel permeated by a solvent. We will then apply the equations to study a possible mechanism for generating the retrograde actin flow in lamellipodia. Finally, we will study the contraction dynamics of an active poroelastic gel.

2 Generalized hydrodynamics of active gels

Generalized hydrodynamics or non-equilibrium thermodynamics provides a general framework for describing systems that are close to thermodynamic equilibrium. In this context, ”close to thermodynamic equilibrium” means that the system is locally at thermodynamic equilibrium, but not globally. As a consequence, one can define a free energy density and locally use the powerful concepts and tools of thermodynamics. In this section, we will sketch the application of this approach to active gels. For a detailed introduction into this topic see, for example, Refs. [12, 13]. A self-contained derivation of the hydrodynamic equations of a one-component polar active gel is given in Ref. [19].

2.1 Hydrodynamic modes

As a consequence of the condition that the system should be locally at thermodynamic equilibrium, only long-lived degrees of freedom are considered within non-equilibrium thermodynamics. These ”hydrodynamic modes” satisfy the condition that their characteristic relaxation time decreases with an increase of the associated wave-number, $\tau \sim k^{-2}$. An example is provided by a particle density c that obeys the diffusion equation, $\partial_t c = D\partial_x^2 c$. A Fourier-transform in space leads to $\frac{\mathrm{d}}{\mathrm{d}t}c_k = -Dk^2 c_k$, such that $c_k \propto \mathrm{e}^{-Dk^2 t}$ and $\tau = D^{-1}k^{-2}$.

Typically, hydrodynamic modes result either from conservation laws as in the above example or from a broken continuous symmetry. For active gels, one typically considers the particle numbers of the gel and the solvent (cytosol), of ATP, ADP, and P$_i$, and momentum as the conserevd quantities. The possible macroscopic orientational order of the actin network is a hydrodynamic mode emerging from a broken continuous symmetry. In the following, we will only consider isotropic cases and do not account for a polar or nematic order parameter. Furthermore, we will consider only systems coupled to a heat bath, such that temperature is constant and energy is not conserved. Finally, we will assume that the concentrations of ATP and of its hydrolysis products are constant in space and time. This is probably appropriate for many reconstituted systems *in vitro*, in case they are endowed with an ATP-regeneration system or for living cells that metabolize nutrients to create ATP. Even if there were spatial or temporal fluctuations in these concentrations, they would be irrelevant as long as the availability of ATP is not rate limiting.

Under these conditions, the relevant dynamic equations for the hydrodynamic modes are

$$\partial_t \rho_{\mathrm{gel}} + \partial_\alpha \rho_{\mathrm{gel}} v_{\mathrm{gel}} = 0 \tag{1}$$

$$\partial_t \rho_{\mathrm{sol}} + \partial_\alpha \rho_{\mathrm{sol}} v_{\mathrm{sol}} = 0 \tag{2}$$

$$\partial_t g_\alpha + \partial_\beta \sigma^{\mathrm{tot}}_{\alpha\beta} = 0. \tag{3}$$

In the two continuity equations for the gel and solvent mass densities, ρ_{gel} and ρ_{sol}, respectively, $\mathbf{v}_{\mathrm{gel}}$ and $\mathbf{v}_{\mathrm{sol}}$ denote the local gel and solvent velocity. In the balance equation for the total momentum $\mathbf{g} = \rho_{\mathrm{gel}}\mathbf{v}_{\mathrm{gel}} + \rho_{\mathrm{sol}}\mathbf{v}_{\mathrm{sol}}$, the total momentum flux tensor σ^{tot} is the same as the mechanical stress tensor. For simplicity, we have set all source and sink terms equal to zero, which amounts to neglecting any bulk exchange between the gel and the solvent and to assuming that there are no bulk external forces. This does not exclude the application of forces or exchange of matter at the surfaces, which are accounted for by boundary conditions. Finally, we have used in these equations Einstein's summation convention for identical indices, for example, $\partial_\alpha v_\alpha = \sum_{\alpha=1}^{3} \partial_\alpha v_\alpha$. Cellular processes typically occur at low Reynolds number, such that inertial terms can eventually be neglected in the momentum balance equation; it then expresses force balance. However, for the time being, the inertial terms are kept to couple the mechanical stress tensor to the dynamics, as we will see in the next section.

To close the dynamic equations, one still needs expressions for the currents. In the framework of non-equilibrium thermodynamics, pairs of conjugated generalized fluxes and forces are identified by considering the entropy production rate. At constant temperature T on can equivalently consider the dissipation rate. The fluxes are then expanded up to linear order in terms of the forces.

2.2 The dissipation rate

At constant temperature, the dissipation rate $\dot{\Theta}$ can be expressed in terms of the free energy:

$$\dot{\Theta} = -\frac{\mathrm{d}}{\mathrm{d}t} \int \mathrm{d}\mathbf{r} \left\{ \frac{g_\alpha^2}{2\rho} + f\left(n_{\mathrm{gel}}, n_{\mathrm{sol}}, n_{\mathrm{ATP}}, n_{\mathrm{ADP}}, n_{\mathrm{P}}\right) \right\}. \tag{4}$$

Here, f is the free energy density and n_i denotes the particle number density of species i with $\rho_{\mathrm{gel}} = m_{\mathrm{gel}} n_{\mathrm{gel}}$ and $\rho_{\mathrm{sol}} = m_{\mathrm{sol}} n_{\mathrm{sol}}$, where m_{gel} and m_{sol} are, respectively, the molecular masses of the gel and the solvent. Here, all components are assumed to be liquids or gases. The cytoskeletal filament network really is a viscoelastic material, such that the free energy density should also depend on the strain tensor u, see below, when the case of a poroelastic gel is treated. The general case of a viscoelastic active gel has been considered in Refs. [20, 21]. For the cytoskeleton in live cells, though, the stress relaxation time is on the order of 10 s. On longer times scales, which are relevant for many cellular processes, it is appropriate to describe the cytoskeleton as a viscous fluid. Returning to Eq. (4), exchanging the time derivative and the spatial integration, using the conservation laws (1)-(3) as well as the Gibbs-Duhem relation $\mathrm{d}P = \sum_i n_i \mathrm{d}\mu_i$, where P is the hydrostatic pressure and $\mu_i = \partial f / \partial n_i$ are the chemical potentials of the various components, we finally arrive at

$$\dot{\Theta} = -\int \mathrm{d}\mathbf{r} \left\{ \sigma^d_{\alpha\beta} v_{\alpha\beta} + j_\alpha \partial_\alpha \bar{\mu} + r\Delta\mu \right\}, \tag{5}$$

where only the relevant terms have been kept. In this expression, σ^d is the deviatory stress with components $\sigma^d_{\alpha\beta} = \sigma^{\mathrm{tot}}_{\alpha\beta} - P\delta_{\alpha\beta}$, where we have now neglected inertial terms and where $\delta_{\alpha\beta} = 1$ if $\alpha = \beta$ and zero otherwise. The components of the symmetric part of the strain rate tensor v are $v_{\alpha\beta} = \left(\partial_\alpha v_\beta + \partial_\beta v_\alpha\right)/2$, where $\mathbf{v}$ is the center-of-mass velocity, $\left(\rho_{\mathrm{sol}} + \rho_{\mathrm{gel}}\right)\mathbf{v} = \rho_{\mathrm{gel}} \mathbf{v}_{\mathrm{gel}} + \rho_{\mathrm{sol}} \mathbf{v}_{\mathrm{sol}}$. The diffusion current $\mathbf{j}$ is defined through $\rho_{\mathrm{gel}} \mathbf{v}_{\mathrm{gel}} = \rho_{\mathrm{gel}} \mathbf{v} + m_{\mathrm{gel}} \mathbf{j}$ and the reduced chemical potential $\bar{\mu} = \mu_{\mathrm{gel}}/m_{\mathrm{gel}} - \mu_{\mathrm{sol}}/m_{\mathrm{sol}}$. Finally, r denotes the ATP-hydrolysis rate and $\Delta\mu = \mu_{\mathrm{ATP}} - \mu_{\mathrm{ADP}} - \mu_{\mathrm{P}}$.

2.3 The constitutive equations

From Equation (5), we identify the generalized fluxes σ^d, $\mathbf{j}$, and r as well as the respective conjugated generalized forces v, $\nabla\bar{\mu}$, and $\Delta\mu$. Expressing the fluxes up to linear order in terms of the forces, we obtain the following constitutive equations

$$\sigma^d_{\alpha\beta} = 2\eta\left(v_{\alpha\beta} - \frac{1}{d}v_{\gamma\gamma}\delta_{\alpha\beta}\right) + \nu v_{\gamma\gamma}\delta_{\alpha\beta} - \zeta\Delta\mu\delta_{\alpha\beta} \tag{6}$$

$$j_\alpha = -\gamma\partial_\alpha\bar{\mu} \tag{7}$$

$$r = \Lambda\Delta\mu + \zeta v_{\gamma\gamma}. \tag{8}$$

The first two terms in Eq. (6) are the usual contributions to the stress of a viscous fluid resulting from pure shear and pure contractile/extensile flows with the corresponding shear viscosity η and the bulk viscosity ν. Furthermore, $\delta_{\alpha\beta}$ is the Kronecker symbol and equates to 1 for $\alpha = \beta$ and to 0 otherwise. Other fluxes and forces of the same tensorial order are coupled by phenomenological constants. Specifically, γ is related to a diffusion constant and Λ determines the hydrolysis rate for a given difference $\Delta\mu$ in the chemical potentials. Most interestingly in the present context, there is a cross-term relating $\Delta\mu$ to the deviatory stress and consequently the rate of strain tensor to the ATP-hydrolysis rate. The coupling coefficient ζ is, up to a sign, the same for both terms as imposed by the Onsager relations.

3 Retrograde flow in lamellipodia

Cells crawling on a solid substrate extend a flat protrusion at the leading edge, the lamellipodium. At the leading edge, the membrane is often pushed forward by polymerizing actin. The cell body follows through actin network contraction induced by myosin motors. It has been observed that relative to the substrate, the actin network in the lamellipodium flows backwards from the leading edge. In this section, we will analyze a cartoon version of the lamellipodium to show that this retrograde flow is a generic consequence of contractile active stresses in the actin network. We will neglect permeation of the solvent and consider an effective one-component description of the gel [21, 22]. This description had been introduced in [23].

3.1 Dynamic equations for an actin slab

We consider an actin slab of fixed height h moving on a substrate that coincides with the (x, y)-plane. Actin polymerizes at x_r at velocity v_p and depolymerizes at x_l at velocity v_d into the direction of positive x, see Fig. 1. The gel assembly dynamics breaks the isotropy of the system by making it globally polar. However, locally the material properties are still isotropic. As we are interested in the behavior on long time scales, we assume the gel to be purely viscous as in the previous section. For simplicity, we will take it to be infinitely compressible.

The only relevant conservation law of the problem is momentum conservation in form of the force balance equation. Given the conditions exposed above, the constitutive equation for the total stress reads

$$\sigma^{\text{tot}}_{\alpha\beta} = \frac{\eta}{2}\left(\partial_\alpha v_\beta + \partial_\beta v_\alpha - \partial_\gamma v_\gamma \delta_{\alpha\beta}\right) + \nu\partial_\gamma v_\gamma\delta_{\alpha\beta} - \zeta\Delta\mu. \tag{9}$$

In the following, we will assume translational invariance in the y-direction. Consequently, the dynamic quantities only depend on x and z.

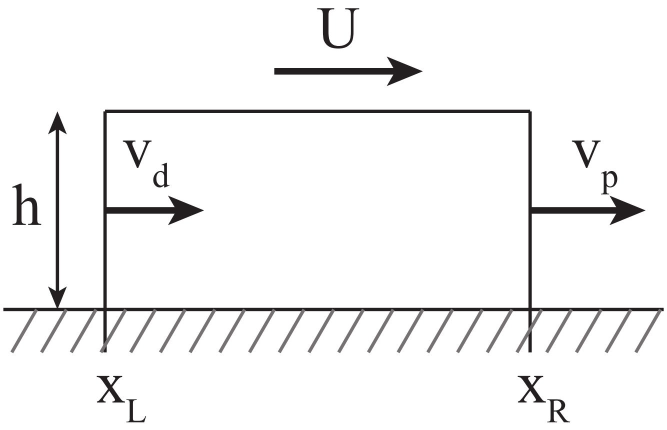

Fig. 1: *Simplified description of a lamellipodium. It is represented by a slab of an active gel with constant height* h*. It polymerizes with velocity* v_p *at* $x = x_r$ *and depolymerizes with velocity* v_d *at* $x = x_l$*. The steady state velocity of the slab is* U*.*

Let us focus on the steady state and look at force balance on a small strip of gel of width Δx. In the x-direction we then get

$$-\int_0^h \sigma_{xx}^{\text{tot}}(x,z)\,dz + \int_0^h \sigma_{xx}^{\text{tot}}(x+\Delta x,z)\,dz \tag{10}$$

$$-\int_x^{x+\Delta x} \sigma_{xz}^{\text{tot}}(x',0)\,dx' + \int_x^{x+\Delta x} \sigma_{xz}^{\text{tot}}(x',h)\,dx' = 0. \tag{11}$$

Note that we have assumed that there are no external bulk forces present. The coupling to the environment is taken into account through the boundary conditions on the stress tensor σ^{tot}. We assume a free boundary at the top of the slab, $z = h$, and friction with the substrate at the bottom, $z = 0$. These boundary conditions, which imply $\sigma_{xz}^{\text{tot}}(x,0) = \xi v_x(x,0)$, where ξ is an effective friction coefficient, and $\sigma^{\text{tot}}(x,h) = 0$, together with the definition

$$\sigma(x) := \frac{1}{h}\int_0^h \sigma_{xx}^{\text{tot}}(x,z)\,dz \tag{12}$$

yield

$$-h\sigma(x) + h\sigma(x+\Delta x) - \xi v(x)\Delta x = 0. \tag{13}$$

Here, we have used $v(x) = v_x(x,0)$. In the limit $\Delta x \to 0$ we arrive at

$$\frac{d}{dx}\sigma = \frac{\xi}{h}v. \tag{14}$$

As the height h is constant and the gel is infinitely compressible, we do not need to consider force balance in z-direction.

From the constitutive equation (9) we obtain

$$\sigma = \tilde{\eta}\frac{d}{dx}v - \zeta\Delta\mu. \tag{15}$$

This completes the definition of the dynamic equations.

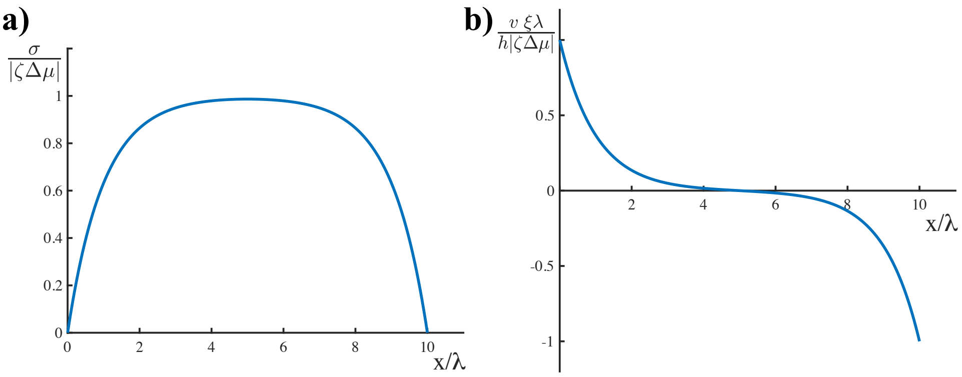

Fig. 2: *Steady state of the actin slab with* $L/\lambda = 10$ *and* $\zeta\Delta\mu < 0$*. Shown are the profiles of the stress (a) and the velocity (b) along the active gel slab.*

3.2 The retrograde flow

Combinig Equations (14) and (15) we get

$$\lambda^2 \frac{d^2}{dx^2}\sigma - \sigma = \zeta\Delta\mu, \tag{16}$$

where the characteristic length λ is determined by $\lambda^2 = \eta h/\xi$. The general solution is given by $\sigma(x) = A\mathrm{e}^{x/\lambda} + B\mathrm{e}^{-x/\lambda} - \zeta\Delta\mu$. We now use the slab's reference frame, such that $x_l = 0$ and $x_r = L$. The integration constants A and B are fixed by the boundary conditions $\sigma(0) = \sigma(L) = 0$ to be

$$A = \zeta\Delta\mu \frac{\mathrm{e}^{-L/\lambda}}{1 + \mathrm{e}^{-L/\lambda}} \tag{17}$$

$$B = \zeta\Delta\mu \frac{1}{1 + \mathrm{e}^{-L/\lambda}} \tag{18}$$

yielding

$$\sigma(x) = \zeta\Delta\mu \left\{ \frac{\cosh \frac{2x-L}{2\lambda}}{\cosh \frac{L}{2\lambda}} - 1 \right\}. \tag{19}$$

For the velocity, which is still measured relative to the substrate, we then have

$$v = \frac{h}{\xi}\frac{d}{dx}\sigma \tag{20}$$

$$= \frac{h\zeta\Delta\mu}{\xi\lambda} \frac{\sinh \frac{2x-L}{2\lambda}}{\cosh \frac{L}{2\lambda}}. \tag{21}$$

For $\zeta\Delta\mu < 0$ we thus obtain a retrograde flow at the leading edge of the slab and an anterograde flow at the trailing edge, see Fig. 2. Note that in absence of active processes, $\Delta\mu = 0$, there are no flows generated.
Let U denote the constant velocity at which the slab is moving. This implies

$$v_{\mathrm{p}} + v(L) = U \tag{22}$$

$$v_{\mathrm{d}} + v(0) = U. \tag{23}$$

These conditions fix the system length L and the velocity U. Explicitly, we have

$$U = \frac{1}{2}\left(v_\mathrm{p} + \mathrm{d}\right) \tag{24}$$

$$L = 2\lambda \mathrm{artanh}\frac{\xi\lambda\left(v_\mathrm{p} - v_\mathrm{d}\right)}{2h\zeta\Delta\mu}. \tag{25}$$

This example shows how the coupling of the chemical energy released during ATP-hydrolysis to mechanical stresses leads to flows of the actin cytoskeleton. Similarly, in confining channels, it can lead to spontaneous laminar [15, 19] and more complex flow patterns [24].

4 Contraction of a poroelastic active gel

In this section, we will study the contraction of an active gel that is permeated by a solvent. Indeed, some works suggest the presence of poroelastic effects in cellular cytoskeletal dynamics [25, 26]. These notably comprise the diffusion of stress and the generation of a solvent flow by a contracting actin network. Such solvent flows might play an important role for distributing proteins and other biomolecules that can, for example, be used for assembling organelles or for signalling purposes. In contrast to the previous examples, we will now consider an elastic active gel.

4.1 The dynamic equations of a poroelastic active gel

Consider an isotropic elastic gel that is permeated by a solvent. There are three conserved quantities in this problem, the gel mass, the solvent mass, and momentum. The respective densities ρ_gel and ρ_sol of the gel and the solvent evolve according to the continuity equations

$$\partial_t\rho_\mathrm{gel} + \partial_\alpha\rho_\mathrm{gel}\dot{u}_\alpha = 0 \tag{26}$$

$$\partial_t\rho_\mathrm{sol} + \partial_\alpha\rho_\mathrm{sol}v_\alpha = 0. \tag{27}$$

Here, $\mathbf{u}$ is the displacement field that describes deformations of the gel from its relaxed state in absence of activity, such that $\dot{\mathbf{u}} \equiv \partial_t\mathbf{u}$ is the gel deformation velocity, and $\mathbf{v}$ the solvent velocity field. To first order in the displacement field, the density ρ_gel can be expressed in terms of the initial gel density ρ_0 at $t = 0$ and the displacement field $\mathbf{u}$ through

$$\rho_\mathrm{gel} = \rho_0\left(1 - \partial_\alpha u_\alpha + \mathcal{O}(u^2)\right), \tag{28}$$

which solves Eq. (26) up to first order in $\mathbf{u}$. Furthermore, the combined gel-solvent system is incompressible, $\rho = \rho_\mathrm{gel} + \rho_\mathrm{sol} = const$, such that the gel volume fraction $\phi \equiv \rho_\mathrm{gel}/\rho$ obeys

$$\partial_\alpha\left(\phi\dot{u}_\alpha + (1-\phi)\,v_\alpha\right) = 0. \tag{29}$$

The material properties are determined by the constitutive equations for the mechanical stress in the system, which enter the momentum conservation equation. This condition reduces again to force balance, because we consider overdamped dynamics, such that inertial terms can be neglected. It determines the gel displacement and solvent velocity fields, such that the dynamics is fully specified. The force balance condition can be written separately for the gel and for the solvent. Explicitly,

$$-\partial_\beta \sigma^{\text{sol}}_{\alpha\beta} = \gamma\left(\dot{u}_\alpha - v_\alpha\right) \tag{30}$$

$$-\partial_\beta \sigma^{\text{gel}}_{\alpha\beta} = -\gamma\left(\dot{u}_\alpha - v_\alpha\right). \tag{31}$$

Here, γ accounts for the friction between the gel and the solvent and has units of a viscosity divided by a length squared. In general, it changes with the gel volume fraction ϕ, but we neglect this dependence for simplicity. The constitutive equations for the gel and solvent stresses result from linear stress-strain and stress-strain rate relations [20, 21]

$$\sigma^{\text{sol}}_{\alpha\beta} = 2\eta v_{\alpha\beta} + P\delta_{\alpha\beta} \tag{32}$$

$$\sigma^{\text{gel}}_{\alpha\beta} = K u_{\gamma\gamma}\delta_{\alpha\beta} + 2\mu\left(u_{\alpha\beta} - \frac{1}{3}\delta_{\alpha\beta}u_{\gamma\gamma}\right) - \zeta\Delta\mu\delta_{\alpha\beta}. \tag{33}$$

The hydrostatic pressure acts as a Lagrange multiplier and is determined by the incompressibility condition. The elastic properties of the dry gel in absence of activity are captured by the constant bulk and shear moduli K and μ. We neglect any direct coupling of the activity, that is, $\Delta\mu$, to the solvent flow.

4.2 Active contraction of a circular symmetric disk

Consider a circular symmetric disk of an active gel embedded in a viscous solvent. We use cylindrical coordinates and neglect any dependence on the angular coordinate θ and the height coordinate z. The relevant components of the stress in the gel are then given by

$$\sigma^{\text{gel}}_{rr} = K\left(\partial_r u_r + \frac{u_r}{r}\right) + 2\mu\partial_r u_r - \zeta\Delta\mu \tag{34}$$

$$\sigma^{\text{gel}}_{\theta\theta} = K\left(\partial_r u_r + \frac{u_r}{r}\right) + 2\mu\frac{u_r}{r} - \zeta\Delta\mu. \tag{35}$$

From these expressions, we obtain the dynamic equation

$$-\gamma\left(\dot{u}_r - v_r\right) = -\left(\nabla\cdot\sigma^{\text{gel}}\right)_r \tag{36}$$

$$= -\left[\partial_r\sigma^{\text{gel}}_{rr} + \frac{1}{r}\left(\sigma^{\text{gel}}_{rr} - \sigma^{\text{gel}}_{\theta\theta}\right)\right] \tag{37}$$

To determine the radial component of the solvent velocity v_r, we use the continuity equation for the total density ρ expressed in terms of the gel volume fraction

$$\frac{1}{r}\partial_r\left(r\phi\dot{u}_r + r\left(1-\phi\right)v_r\right) = 0. \tag{38}$$

We consider a situation, where the gel is embedded in a circular recipient, such that the total material flux at the boundary of the system equals zero. Hence, the continuity equation yields

$$v_r = -\frac{\phi}{1-\phi}\dot{u}_r. \tag{39}$$

The solvent flow is always directed opposite to the gel displacement velocity. For a gel volume fraction $\phi > 1/2$, the solvent flow is faster than the gel displacement velocity.

According to Equation (28), the gel volume fraction can be expressed in terms of the initial gel volume fraction ϕ_0 and the radial gel displacement field u_r. Using this relation and expression (39) for v_r we can rewrite the dynamic equation (37) in a form that only depends on the displacement vector field u_r:

$$\dot{u}_r = \frac{1-\phi}{\gamma}\partial_r \left[(K+2\mu)\left\{\partial_r u_r + \frac{u_r}{r}\right\} - \zeta\Delta\mu\right]. \tag{40}$$

Finally, we have to specify the boundary conditions. In the center, clearly $u_r\,(r=0)=0$. Furthermore, we assume that there are no external forces applied to the border of the gel and the corresponding boundary conditions read $\sigma_{rr}^{\mathrm{gel}}\,(r=R+u_r(R))=0$ and $\sigma_{\theta\theta}^{\mathrm{gel}}\,(r=R+u_r(R))=0$. Here, R is the initial and $R+u_r(R)$ the current radius of the gel. The homogenous active stress $-\zeta\Delta\mu$ only contributes at the boundary. Consequently, we can absorb it into a boundary condition and solve

$$\dot{u}_r = \frac{1-\phi}{\gamma}\partial_r \left[(K+2\mu)\left\{\partial_r u_r + \frac{u_r}{r}\right\}\right] \tag{41}$$

with $(K+2\mu)\left\{\partial_r u_r + \frac{u_r}{r}\right\}\big|_{r=R} = \zeta\Delta\mu$.
In the following, we will scale space with the initial radius R, time with $\gamma R^2/\,(K+2\mu)$, and stresses with $K+2\mu$. Consequently, the system dynamics depends only on two dimensionless parameters: the initial gel volume fraction ϕ_0 and the dimensionless active stress $\zeta\Delta\mu$, for which we have kept the original notation. Anticipating that the solution of the dynamic equation for $\zeta\Delta\mu<0$ describe contraction of the gel, we note that the scaling implies that the maximal contraction velocity scales inversely proportionally with the initial system size whereas the characteristic relaxation time scales with R^2. The latter is consistent with observations of contracting actomyosin networks *in vitro* [27].
The steady state, $\dot{u}_r=0$ is given by

$$u_r^{(0)}(r) = \frac{\zeta\Delta\mu}{2}r, \tag{42}$$

such that the final strain is proportional to the activity. The gel density as well as the stress are homogenous in the steady state: the gel volume fraction equals $\phi_0(1-\zeta\Delta\mu)$ and the total stress vanishes.

4.3 The limit of small deformations

In general, the dynamic equation (41) is difficult if not impossible to solve analytically. In case the overall deformation of the gel is small, changes in the gel volume fraction ϕ can be neglected. In the dynamic equation (41), we can then set $\phi=\phi_0$ leaving us with a linear equation:

$$\dot{u}_r = (1-\phi_0)\,\partial_r\left(\partial_r u_r + \frac{u_r}{r}\right). \tag{43}$$

The boundary condition is $\left(\partial_r u_r + \frac{u_r}{r}\right)\big|_{r=1} = \zeta\Delta\mu$. The radial deformation field is thus determined by the diffusion equation, which depends only through the boundary condition on the active stress $\zeta\Delta\mu$.

To solve the linearized dynamic equation, we write $u_r(r,t) = u_r^{(0)}(r) + w(r,t)$. The function w then also obeys Eq. (43), but now with the boundary condition $\left(\partial_r w + \frac{w}{r}\right)\big|_{r=1} = 0$. Using the separation *ansatz* $w(r,t) = T(t)\Psi(r)$. We obtain

$$T = \mathrm{e}^{-(1-\phi_0)\omega t} \tag{44}$$

$$\frac{\mathrm{d}}{\mathrm{d}r}\left(\Psi' + \frac{\Psi}{r}\right) = -\omega\Psi, \tag{45}$$

where the prime indicates derivation with respect to r. The solution to the second equation is given by $J_1(\sqrt{\omega}r)$, where J_1 is the Bessel function of the first kind. The possible values of ω are determined by the boundary conditions, that is,

$$\sqrt{\omega}J_1'(\sqrt{\omega}) + J_1(\sqrt{\omega}) = 0. \tag{46}$$

Under this condition, the Bessel functions are pairwise orthogonal:

$$\int_0^1 J_1(\sqrt{\omega}r)J_1(\sqrt{\omega'}r)\; r\mathrm{d}r = \delta_{\omega\omega'}. \tag{47}$$

The general solution to Eq. (45) is then given by

$$w(r,t) = \sum_{j=1}^{\infty} a_j \mathrm{e}^{-(1-\phi_0)\omega_j t} J_1(\sqrt{\omega_j}r), \tag{48}$$

where ω_j denote the possible solutions of Eq. (46) and where the values a_j, $j = 1, \ldots$ are determined by the initial condition $w(r, t = 0) = w_{\text{init}}(r) \equiv u_{r,\text{init}} - u_r^{(0)}$ through

$$a_j = \int_0^1 w_{\text{init}}(r)J_1(\sqrt{\omega_j}r)r\;\mathrm{d}r \Big/ \int_0^1 J_1^2(\sqrt{\omega_j}r)r\;\mathrm{d}r. \tag{49}$$

For sufficiently small values of $\zeta\Delta\mu$, the system is always in the limit of small deformations and its dynamics is completely specified by the above solution, see Fig. 3a. Eventually, the relaxation occurs with a critical time scale $\omega_1^{-1}\left(1-\phi_0\right)^{-1}$, where ω_1 is the smallest non-zero positive solution to Eq. (46).

4.4 Large deformations

In the general case of arbitrary radial deformations, the dynamic equation (41) is nonlinear and we have to resort to numerical solutions. For the numerical solution of the dynamic equations we use an explicit forward Euler method. The discretization scheme is detailed in App. A.

For small activities, the solution of the full equation agrees well with the linearized equation (43), see 3a. In the general case, initially the contraction is too slow, see Fig. 3b. The numerical solution shows that contraction starts always from the boundary, see Fig. 4. This was to be expected, because the active stress is unbalanced only there. The displacement and hence the stress in the gel then propagate towards the center of the disk according to the diffusion equation (41) with a state dependent diffusion constant. Together with the generation of a solvent flux, this is one of the hall marks of poroelasticity.

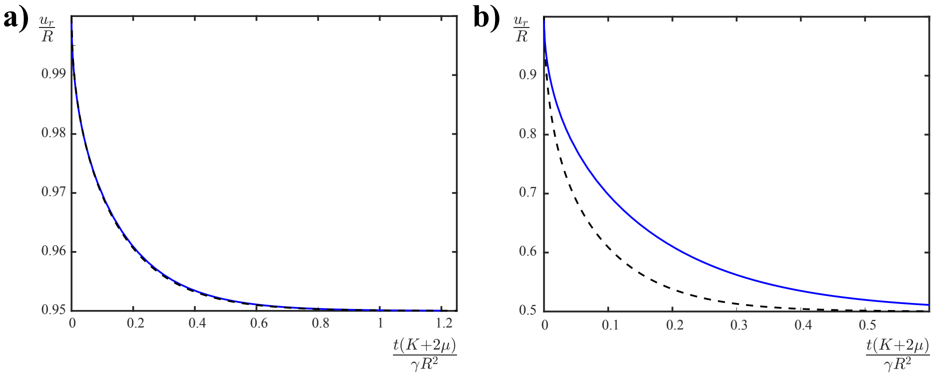

Fig. 3: *Radius of a contracting poroelastic disk as a function of time for small activity* $\zeta\Delta\mu = -0.1$ *(a) and large activity* $\zeta\Delta\mu = -1$ *(b). Shown are the solution of the linearized dynamic equation (blue solid line) and of the full dynamic equation that is numerically integrated (black dashed line). The initial gel volume fraction is* $\phi_0 = 0.01$.

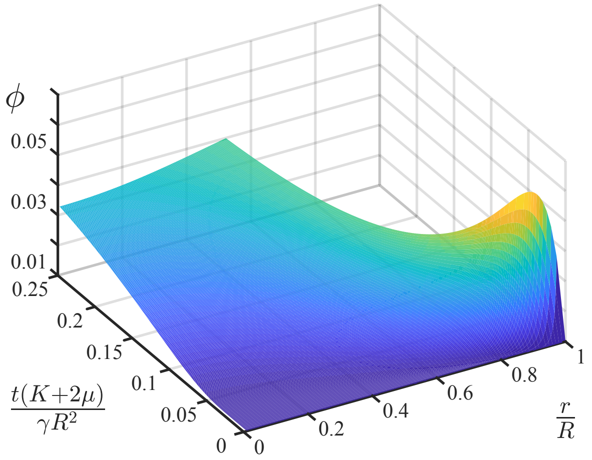

Fig. 4: *The gel volume fraction as a function of space and time for the same parameters as in FIg. 3b.*

5 Conclusions

In this chapter, we have sketched the derivation of the hydrodynamic equations for isotropic active gels and discussed two examples of spontaneously emergent gel flows. These flows were due to contractile stresses generated by active processes that are driven by the hydrolysis of ATP. Since we restricted attention to isotropic gels without any polar order, the active stress only entered the description through the boundary conditions. In the general case, the active stress is anisotropic and its components change with changing polar (or nematic) order. In that case, much richer spontaneous flow patterns can be observed [2, 24]. They are tightly connected to the emergence of topological point defects. For high enough activity, one can even observe low Reynolds number turbulence, that is, spatiotemporal chaos.

Even though the generalized hydrodynamic equations for active gels are *a priori* only valid on macroscopic length scales, this approach has been successfully applied to describe subcellular dynamics, notably, the formation and contraction of actomyosin rings during cell division [17]. It will be interesting to see other applications in the future, in particular, through coupling active gel theory to cell signaling pathways. Since it is based on symmetries rather than molecular processes, active gel theory can and has been applied to tissue dynamics. In particular, in the context of embryonic development, a number of interesting phenomena wait to be analyzed in this framework.

Appendices

A Discretization scheme for the numerical solution of the active poroelastic dynamic equations

In this appendix, we explicit the discretization scheme, we used to solve the dynamic equation (41) for the radial displacement field. We introduce a dynamic lattice carrying the gel. Its sites are given by $i\Delta r + u_i$, $i = 0, \dots, N$ with $N = 1/\Delta r$. Here u_i is the radial displacement vector at $i\Delta r$. The gel volume fraction and the stresses are associated with the bonds between the lattice sites. We will, respectively, denote them by $\phi_{i-\frac{1}{2}}$, $\sigma_{rr,i-\frac{1}{2}}$, and $\sigma_{\theta\theta,i-\frac{1}{2}}$ for the bond between sites i and $i-1$.

For calculating the gel volume fraction for a given displacement field, we do not take the approximate form given in Eq. (28), but the exact form that is obtained from equating the gel mass in a volume element before and after deformation. It yields for $i = 2, \dots, N$

$$\phi_{i-\frac{1}{2}} = \phi_0 \frac{(2i-1)\,\Delta r^2}{[(2i-1)\,\Delta r + u_i + u_{i-1}]\,[\Delta r + u_i - u_{i-1}]} \tag{50}$$

and

$$\phi_{\frac{1}{2}} = \phi_0 \frac{\Delta r^2}{(\Delta r + u_1)^2}. \tag{51}$$

For the stresses, Eqs. (34) and (35) lead to

$$\sigma_{rr,i-\frac{1}{2}} = \left(\frac{u_i - u_{i-1}}{\Delta r}\right) + \frac{u_i + u_{i-1}}{(2i-1)\,\Delta r} - \zeta\Delta\mu \tag{52}$$

$$\sigma_{\theta\theta,i-\frac{1}{2}} = \left(\frac{u_i - u_{i-1}}{\Delta r}\right) + \frac{u_i + u_{i-1}}{(2i-1)\,\Delta r} - \zeta\Delta\mu \tag{53}$$

for $i = 2, \ldots, N$ and

$$\sigma_{rr,\frac{1}{2}} = \frac{u_1}{\Delta r} + \frac{u_1}{\Delta r} - \zeta\Delta\mu \tag{54}$$

$$\sigma_{\theta\theta,\frac{1}{2}} = \frac{u_1}{\Delta r} + \frac{u_1}{\Delta r} - \zeta\Delta\mu \tag{55}$$

$$\sigma_{rr,N+\frac{1}{2}} = \sigma_{\theta\theta,N+\frac{1}{2}} = 0, \tag{56}$$

where we have used the dimensionless form introduced in the main text. Then, the time evolution is given by

$$\dot{u}_i = \left(1 - \frac{\phi_{i-\frac{1}{2}} + \phi_{i+\frac{1}{2}}}{2}\right)\left\{\frac{\sigma_{rr,i+\frac{1}{2}} - \sigma_{rr,i-\frac{1}{2}}}{\Delta r + \frac{u_{i+1}+u_{i-1}}{2}} + \frac{1}{2}\frac{\sigma_{rr,i+\frac{1}{2}} + \sigma_{rr,i-\frac{1}{2}} - \sigma_{\theta\theta,i+\frac{1}{2}} - \sigma_{\theta\theta,i-\frac{1}{2}}}{i\Delta r + u_i}\right\} \tag{57}$$

for $i = 1, \ldots, N$ if we set $u_0 = u_{N+1} = 0$.
Finally, we use mass conservation, Eq. 39, to obtain the radial solvent velocity. The corresponding discretized field $v_{i-\frac{1}{2}}$ gives the solvent velocity at $\left(i - \frac{1}{2}\right)\Delta r$ for $i = 1, \ldots, N$. It can be computed directly from $\phi_{i-\frac{1}{2}}$ and $\dot{u}_i$. Explicitly

$$v_{i-\frac{1}{2}} = -\frac{\phi_{i-\frac{1}{2}}}{1 - \phi_{i-\frac{1}{2}}}\frac{\dot{u}_{i-1} + \dot{u}_i}{2} \tag{58}$$

for $i = 1, \ldots, N$. Outside of the gel, the solvent velocity vanishes, $v_{i-\frac{1}{2}} = 0$ for $i \geq N + 1$.

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