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Activity pulses induce spontaneous flow reversals in viscoelastic environments

Emmanuel L. C. VI M. Plan1,2, Julia M. Yeomans3 and Amin Doostmohammadi4

1Institute of Theoretical and Applied Research, Duy Tan University, Ha Noi 100 000, Viet Nam
2Faculty of Natural Science, Duy Tan University, Da Nang 550 000, Viet Nam
3The Rudolf Peierls Centre for Theoretical Physics, Department of Physics, University of Oxford, Clarendon Laboratory, Oxford OX1 3PU, UK
4The Niels Bohr Institute, University of Copenhagen, Blegdamsvej 17, 2100 Copenhagen, Denmark

ELCVIMP, 0000-0003-2268-424X; JMY, 0000-0001-8268-5469; AD, 0000-0002-1116-4268

Complex interactions between cellular systems and their surrounding extracellular matrices are emerging as important mechanical regulators of cell functions, such as proliferation, motility and cell death, and such cellular systems are often characterized by pulsating actomyosin activities. Here, using an active gel model, we numerically explore spontaneous flow generation by activity pulses in the presence of a viscoelastic medium. The results show that cross-talk between the activity-induced deformations of the viscoelastic surroundings and the time-dependent response of the active medium to these deformations can lead to the reversal of spontaneously generated active flows. We explain the mechanism behind this phenomenon based on the interaction between the active flow and the viscoelastic medium. We show the importance of relaxation time scales of both the polymers and the active particles and provide a phase space over which such spontaneous flow reversals can be observed. Our results suggest new experiments investigating the role of controlled pulses of activity in living systems ensnared in complex microenvironments.

1. Introduction

The study of biological systems as active materials has made tremendous advances in the past decades [1–5]. The ‘activity’ describes the ability of living systems to extract chemical energy from their surrounding environment and convert it into mechanical work. This happens at the level of individual constituents of the matter in, for example, sperm cells thrusting forwards by the rotation of their flagella, bacterial self-propulsion, eukaryotic cells migrating within extracellular networks and the cytoskeletal machinery inside cells that is powered by motor proteins. As such, the overarching theme in various kinds of living systems is the local activity generation that drives the entire system far from thermodynamic equilibrium, resulting in the collective patterns of motion observed in cellular tissues, bacterial colonies and sub-cellular flows [3,6,7].

The cross-talk between the mechanical micro-environment of living matter and this intrinsic ability of living systems to actively generate self-sustained motion governs pattern formation and self-organization in important biological processes including collective transport of sperm cells in confined tubes [8], shaping bacterial biofilms [9,10], tissue regeneration [11] and sculpting organ development [12]. Not only does the mechanical micro-environment provide geometrical constraints for active materials [13], but it is also often endowed with viscoelastic properties that allow for time-dependent responses to activity-induced stresses and deformations [2,14]. Significant examples are the extracellular matrices, surrounding cells and tissues that play a key role in cell death and proliferation, stem cell differentiation, cancer migration and cell response to drugs [15]. It is thus

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essential to understand the dynamic interconnection between
the activity-induced stresses and the mechanical response of
the viscoelastic medium.

Indeed, several recent studies have made the first attempts in
this direction, showing that accounting for viscoelastic effects
of the medium around living matter results in significant modi-
cation in the patterns of motion generated by continuous
activity-induced stresses [16–22]. Importantly, however, in var-
iou previous contexts the activity generation is not constant
and continuous, but rather is characterized by changes in the
activity level and even activity pulses. Striking examples are the
presented in §3. Finally, concluding remarks and a discussion
of flow reversal and its associated phase space are
results of the simulation together with the physical mechan-
isms of flow reversal and shows its dependence on the relevant
time scales through a stability diagram.

In order to investigate the fundamental impact of activity
pulses, we employ a continuum model of active matter based
on the theory of active gels, which has proven very successful
in describing several aspects of the physics of active systems
including actomyosin dynamics at the cell cortex [5,26],
actomyosin-induced cell motility [27,28], actin retrograde
flows [29,30] and the topological characteristics of actin fila-
ments [31,32]. One important prediction of active gel models
is the emergence of spontaneous flow generation in a confined
active gel [33], which has been further experimentally validated
in different biological systems [34,35] and is a generic feature of
confined active materials. Here, we consider a simplified set-up
of an active gel confined within viscoelastic surroundings and
study the emergence of a spontaneous flow by introducing
activity pulses and varying the relaxation time of the viscoelastic
medium. We show that introducing activity pulses can result in
the reversal of the spontaneous flow direction accompanied by
the rearrangement of the orientation of active constituents. The
mechanistic basis for this reversal is explained based on the feed-
back between the active flows and the viscoelastic deformation,
particularly in between activity pulses. We further provide a
simple model that reproduces the essential dynamics of the
flow reversal and shows its dependence on the relevant time
scales through a stability diagram.

The paper is organized as follows. In §2, we describe the
details of the simulation set-up and introduce the governing
equations of motion for the active gel, the surrounding visco-
elastic medium and the coupling between the two. The
results of the simulation together with the physical mechan-
ism of flow reversal and its associated phase space are
presented in §3. Finally, concluding remarks and a discussion
of the broader impacts of the results are provided in §4.

2. Methods
The active gel is simulated in two dimensions as a horizontal
stripe within a passive viscoelastic region, and is differentiated
via an indicator function \( \phi \) whose value is \( \phi = 1 \) in the active
region and \( \phi = 0 \) in the passive viscoelastic region. The indicator
function \( \phi \) is only defined to distinguish between the active and
passive regions and as such it is fixed, without any dynamical
activity. Activity and viscoelasticity are incorporated by intro-
ducing a generic two-phase model of active matter in viscoelastic
domains [22,26], which is summarized below.

2.1. Active region
Following its success in describing the dynamics of the cell cyto-
skeleton, bacterial colonies and confluent cell layers, we use
liquid crystal nematohydrodynamics to model the active region
[4,37,38]. Within this framework, each active particle generates
a dipolar flow field with the axis along its direction of alignment.
The alignment direction is nematic, i.e. it has a head–tail sym-
metry. This can be captured at a coarse-grained level by the
order parameter tensor \( Q \) through its principal eigenvector,
which describes the nematic director orientation, and the associated
eigenvalue, which describes the degree of alignment.

The free energy \( f_Q \) for two-phase nematic models follows the
Landau–De Gennes description

\[
f_Q = A_Q \left[ \frac{1}{2} \left( 1 - \frac{\eta f}{3} \right) \text{Tr}[Q^2] - \frac{\eta f}{3} \text{Tr}[Q^2] + \frac{\eta f}{4} \text{Tr}[Q^2]^2 \right] + \frac{K_Q}{2} \nabla(Q)^2 + D_Q \nabla^2(Q),
\]

(2.1)

where \( A_Q \) describes the stability of the nematic or isotropic con-
figurations, with the former being favoured when \( \eta \geq 2.7 \). The
elastic coefficient \( K_Q \) penalizes gradients in \( Q \), and a positive
(negative) \( D_Q \) enforces nematic orientation parallel (perpendicular)
to the active–viscoelastic interface.

In the presence of a velocity field \( u \), the nematic tensor is
evolved according to the equation \( \partial_t Q + u \cdot \nabla Q = Q_0 + \Gamma C H_Q \),
where the left-hand side is the usual material advective
derivative. The co-rotational term \( Q_0 = (\partial_t + u)Q + (Q + 1/3)\partial_i Q\partial^i Q \)
describes nematic reorientation in response to both vorticity \( \Omega \)
and flow strain \( D \), with the tumbling parameter \( \xi \) determining whether the directors
align or tumble in the flow. \( H_Q \) controls the speed of relaxation
towards the free energy minimum determined by the molecular
field \( H_0 = -\nabla f/\nabla Q \). The typical nematic relaxation time scale \( \tau_0 \)
when confined in a channel of width \( W \) is given by \( W^2/\Gamma C H_Q \)
and the dynamical equation for \( Q \) can thus be rewritten as

\[
\partial_t Q + u \cdot \nabla Q = Q_0 + \left( \frac{W^2}{\Gamma C H_Q} \right) H_Q.
\]

(2.2)

Since individual components of the active region generate
dipolar forces with the axis along their direction of alignment, the
corresponding active stress is proportional to the orientation
tensor \( [1,30,37] \)

\[
\sigma_{\text{active}} = -\xi f Q,
\]

such that gradients in the orientation field induce forces on the fluid
and drive active flows. The activity parameter, \( \xi \), measures the
strength of the active driving.

2.2. Viscoelastic region
The passive region is endowed with viscoelasticity that is
defined by the conformation tensor \( C \), which characterizes
the polymer orientation by its principal eigenvector, and the
(square of the) polymer length, by its trace. Here we use the Old-
royd-B model to reproduce simple viscoelastic effects, i.e.
polymer relaxation is linear with respect to the elongation and
is governed by a single relaxation time \( \tau \) [39].

The free energy associated with an Oldroyd fluid

\[
f_C = A_C \left( 1 - \frac{\delta f}{2 \ln |C|} \right),
\]

governs the polymer relaxation to its unstretched equilibrium \( C = I \)
(2.4)

where \( \delta f/\delta C \) appears in the dynamical equation governing the
evolution of \( C \). \( \partial_t C + u \cdot \nabla C = S_C + \Gamma C', H_T C + C' H_T C \), where \( \Gamma \)

The power law exponent associated with the advection of
the polymer conformation \( C \), its response to velocity gradients
through \( S_C = C \partial_t C - \Omega C + \partial_t C + D'C^T \) and its relaxation to
When activity is turned off, the polymers relax and create a weaker but reversed flow, which reorients the directors. Within the passive region (where the Oldroyd-B model is used), the polymer contribution to the stress is 

\[ \sigma_{\text{polymer}} = A_C(1 - \phi)(C - D), \]  

(2.6)

where the factor \( 1 - \phi \) ensures that the polymer stress only acts within the passive region (where \( \phi = 0 \)).

### 2.3. Coupling and simulation details

The active and viscoelastic regions interact with each other through the incompressible velocity field \( u \), which obeys the Cauchy momentum equation

\[ \rho \partial_t u + u \cdot \nabla u = -\nabla p + \nabla \cdot \sigma \quad (\nabla \cdot u = 0), \]  

(2.7)

where \( \rho \) is the fluid density, \( p \) is the pressure and \( \sigma \) is the sum of viscous, capillary, elastic, active (equation (2.3)) and polymer (equation (2.6)) stresses. The other stresses take the forms [22]:

\[ \sigma_{\text{viscous}} = 2\nu \mathbf{D}, \quad \sigma_{\text{capillary}} = (f - \phi \mu) \mathbb{I} - K_\phi (\nabla \phi) \otimes (\nabla \phi) - 2L_\phi (\nabla \phi \cdot \nabla \phi), \quad \sigma_{\text{active}} = -\phi \mathbb{I}, \]  

and

\[ \sigma_{\text{polymer}} = -\xi H_\phi (Q + \frac{1}{3} \mathbb{I}) - \phi [\frac{1}{2} \mathbb{I} + J_\phi H_\phi \mathcal{Q} - 2\xi \mathcal{T} (Q + \frac{1}{3} \mathbb{I}) + \mathcal{Q} H_\phi - H_\phi Q - K_Q (\nabla \mathcal{Q}) : (\nabla \mathcal{Q})]. \]  

Here, \( f \) is the total free energy, \( \mu = -\partial f / \partial \phi \) is the molecular potential and \( K_\phi \) is a parameter controlling the active–polymeric interface width. Both the active and viscoelastic regions exert stresses on the fluid, and the resulting velocity field couples the two regions through advective and co-rotational terms in equations (2.2) and (2.5).

Equations (2.2), (2.5) and (2.7) are evolved using a hybrid lattice Boltzmann method [40,41]. The simulation domain has dimensions \( L \times H \), is periodic in the \( x \)-direction and has no-slip boundary conditions in the \( y \)-direction (see schematic in figure 1a), as in typical experimental and numerical studies of active matter (e.g., [14]). The dynamics is not affected by the length of the channel \( L \), because of periodicity; our results here use \( L = 10, H = 100 \). The width of the active region is fixed at \( W = 20 \).

In order to obtain a unidirectional flow, the parameters for the active region are chosen to be \( A_Q = 1.0 \) and \( K_Q = 0.2 \), and we use \( \xi = 0.7 \) corresponding to the flow-aligning regime as previous studies of confined active nematics have shown that a unidirectional shear-like flow of active nematics in a confined channel can only be achieved for flow alignment [42]. \( \eta(\phi) \) is chosen such that \( \eta = 2.95 \) within the active region \( \phi = 1 \) [42], while the passive viscoelastic region, \( \phi = 0 \), is in the isotropic...
phase with $\eta < 2.7$. The polymer contribution to viscosity is fixed at $\nu = 1$ and $A_c = 1/\tau$. The values of the flow parameters are $p = 1$, $p = 0.25$, and the Newtonian contribution to the viscosity is $\nu_{\text{flow}} = 2/3$. We also enforce weak nematic anchoring at the boundary, $L_0 = 0.05$, for stability. This was verified to have no qualitative effect on the flow reversal dynamics.

Each simulation begins with equilibrated polymers $C = 1$ and nematic directors with small random perturbations about the $x$-axis. Active stresses are applied until the system establishes a steady-state, unidirectional flow, after which the activity is temporarily turned off at $t_{\text{off}} = 10^3$ for a duration of $d = t_{\text{on}} - t_{\text{off}}$ time steps. The equations are solved until the flow is re-established.

### 3. Results

When activity is turned off at a time $t_{\text{off}}$ and turned back on at a time $t_{\text{on}}$, the flow is re-established in the same or, surprisingly, in the opposite direction. This is not a random choice but depends sensitively on the parameters setting the relevant nematic and viscoelastic time scales. For example, the movie provided as electronic supplementary material shows several successive reversals in the direction of the velocity. We first explain how this dependence comes about, and then present a simple model which illustrates the underlying physics. The mechanism of the flow reversal is summarized in figure 1b–d.

Figure 2. Emergence of spontaneous flow reversals. (Top) The mean velocity $\langle u_x \rangle_{\text{act}}$ in the active stripe, (middle) the nematic angle at the interface $\theta_i$ as a function of time for the full simulations ($t_n = 4000$) and (bottom) the nematic angle for the simplified model ($t_n = 150$). (a) Black: no polymers, activity switching time $d = 10^3$; (b) red: activity switching time $d = 10^4$, polymer relaxation time $\tau = 10^4$; (c) dashed: activity switching time $d = 5000$, polymer relaxation time $\tau = 10^4$; (d) blue: activity switching time $d = 5000$, polymer relaxation time $\tau = 3000$. The cyan curves show the behaviour in the absence of reactivation. (e) Red: activity switching time $d = 400$, polymer relaxation time $\tau = 600$; (f) dashed: activity switching time $d = 200$, polymer relaxation time $\tau = 600$; (g) blue: activity switching time $d = 200$, polymer relaxation time $\tau = 300$. The insets show a zoom-in on the period of inactivity and immediately after reactivation.

Figure 2 shows the variation of the mean velocity in the channel, $\langle u_x \rangle$, and the angle $\theta_i$ that the mean director field at the interface makes with the channel axis as a function of time for selected simulation parameters. Consider first figure 2a where there are no polymers in the passive region. Activity is switched on at time $t = 0$. This drives the active nematic instability and active stresses resulting from gradients in the director field set up a linear flow along the stripe. The spontaneous flow is stabilized by the channel interfaces, and the resulting steady-state flow profile corresponds to directors aligning at the Leslie angle to the local shear [43,44]. When the activity is switched off the flow...
decays faster than the relaxation time of the nematic director. In the absence of polymers, if activity is switched back on before the end of the decay the residual director rotation ensures that the flow re-starts in the same direction as before.

The presence of polymers changes the response of flow to activity pulses. In figure 2b–d, the passive medium is viscoelastic and the shear flow induced by the activity stretches the polymers, thus storing energy. The initial build-up of the flow is similar to the no polymer case, but slower, as work is done to stretch the polymers, and the steady-state value of the flow in the channel is lower because the polymers impose stresses that oppose the flow. This also means that after 1off the decays of the velocity and director fields to equilibrium are faster and, in particular, stress imposed by the relaxation of the surrounding polymers may be strong enough to reverse the flow in the channel.

For example in figure 2b both the residual flow and the director have reversed at 1on, making a velocity reversal inevitable. By comparison, for the same polymer relaxation time but faster switching of activity in figure 2c, at 1on the director distortion is still just positive but the velocity has been reversed by the polymer stresses. The activity tries to rebuild the flow in the original direction whereas the remaining elastic energy stored in the surrounding polymers pushes the fluid in the opposite direction. The flow slowly reverses as the instability is (just) overcome by the residual polymer stresses. The director distortion reverses and the velocity slowly increases until it eventually attains its steady-state value, but in the opposite direction. By contrast, figure 2d shows an example of faster polymer relaxation, compared with figure 2c, where the polymer stress is not sufficiently strong to cause flow re-orientation and both nematic directors and mean velocity regain their original direction.

Such a flow reversal mechanism that depends on stored polymer stresses and residual director orientation implies that the relevant time scales here are the polymer relaxation time 1p, the nematic relaxation time 1n, and the period of inactivity 1 = 1on − 1off. To further explain the phenomenon of flow reversal and highlight the competition between these varying time scales, we construct simplified, space-independent, dynamic equations for the evolution of the active nematic and polymeric particles.

To this end, we consider the dynamics of the alignment for the angles θn, θp formed by the active nematic directors and the polymer directors, respectively, with respect to the direction of a simple shear flow, u = (γy, 0) [45],

\[
\frac{d\theta_n}{dt} = \gamma \xi_n \cos 2\theta_n \frac{1}{1 + \frac{\theta_n}{\tau_n}}
\]

and

\[
\frac{d\theta_p}{dt} = \gamma \xi_p \cos 2\theta_p \frac{1}{1 + \frac{\theta_p}{\tau_p}}.
\]

These equations are approximations of the orientation of rod-like particles with tumbling parameters \(\xi_n, \xi_p\) in response to a shear flow with rate \(\gamma\). In the absence of shear, \(\gamma = 0\), the angles will relax exponentially to zero.

A time-dependent shear rate \(\gamma\) couples the two equations and can be determined from balancing the viscous stress, \(\sigma_{\text{viscous}} = 2\nu_0 \dot{\gamma} \mathbf{D}\), with the active (equation (2.3)) and polymer (equation (2.6)) stresses. Solving for the off-diagonal of the rate of strain tensor \(\mathbf{D}\) and constructing the tensors \(Q_{ij} = n_i n_j - \delta_{ij}/2\) and \(C_{ij} = p_i p_j\) from the unit directors \(n = (\cos \theta_n, \sin \theta_n)\) (and analogously for \(p\)), we obtain the simple time-dependent shear

\[
\dot{\gamma} = \frac{1}{2\nu_0} \left( \xi Q_{yy} - \frac{\nu}{7} C_{yy} \right) = \frac{1}{4\nu_0} \left( \xi \sin 2\theta_n - \nu \sin 2\theta_p \right),
\]

in terms of the nematic and polymer directors. For simplicity, we fix \(\nu_0 = 2/3, \nu = 1\) and set \(\xi_n = 1.1\) and \(\xi_p = 0.275\) and take initial conditions \(\theta_n = \theta_p = 0.01\).

It is clear from (3.3) that, when the activity \(\xi = 0\) is turned off, the flow reverses in the opposite direction owing to the presence of the polymers. Moreover, a simulation of this simplier set of equations features the same essential reason for the reversal as in the full simulations: there exists sufficient polymer stress to reorient the nematics during the period between activity pulses. Figure 2c–g shows that the nematic angle \(\theta_n\) exhibits trajectories similar to the result from the full equations of motion, figure 2b–d. The reversed flow can drive the nematic angle negative during the period of inactivity, which is a sufficient condition for flow reversal. Moreover, even if \(\theta_n\) remains positive when the activity is switched on, the polymer stress can still overcome the activity (i.e. \(\xi \sin 2\theta_n < \nu \sin 2\theta_p / \tau\)) and continue to drive the nematic director to reverse direction.

Using the simple model, we examined the phase space of flow reversal for varying time scales of nematic and polymer relaxations, \(1_n\) and \(\tau\), respectively, as well as the activity switching time \(1 = 1on - 1off\) (figure 3a). In particular, we observe that the reversal can be ensured if three dimensionless ratios are sufficiently large:

(i) \(d/1_n\): nematic directors have enough time to relax.
(ii) \(\tau/1_n\): polymers retain enough energy to reverse nematic orientation when \(\theta_n \approx 0\).
(iii) \(d/1_n^2\): residual polymer stress at the moment of reactivation can help reverse nematic orientation if condition (i) alone is insufficient.

These three constraints are illustrated as dashed black lines on the flow reversal phase diagram in the \(d/1_n - \tau/1_n\) phase space and clearly distinguish the parameter space with (blue markers) and without (red markers) flow reversal.

We also plot, in figure 3b, the similar phase diagram obtained from full simulations of the active gel surrounded by a viscoelastic medium showing close qualitative agreement with the simple model, and indicating that the parameter region for flow reversal is suitably captured by these three constraints. The quantitative difference between the simplified model and the full simulations is expected because in the simplified model there is no space dependence and we only account for polymer orientation in the polymer stress, whereas the full simulations are space dependent and have a polymer stress (equation (2.6)) that depends on polymer elongation, which is higher when \(\tau\) is larger. Notwithstanding these limitations, the close qualitative agreement of the angle profiles and the phase diagram obtained from the simple model with those from the full hydrodynamic simulations of spatio-temporal evolution of the active nematics and polymeric fluids confirms the importance of the time-scale constraints for the flow reversal and the underlying physics of stress balance during the period of inactivity.
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