Three-dimensional chiral morphodynamics of chemomechanical active shells
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Edited by David Weitz, Harvard University, Cambridge, MA; received April 8, 2022; accepted October 26, 2022

Morphogenesis of active shells such as cells is a fundamental chemomechanical process that often exhibits three-dimensional (3D) large deformations and chemical pattern dynamics simultaneously. Here, we establish a chemomechanical active shell theory accounting for mechanical feedback and biochemical regulation to investigate the symmetry-breaking and 3D chiral morphodynamics emerging in the cell cortex. The active bending and stretching of the elastic shells are regulated by biochemical signals like actomyosin and RhoA, which, in turn, exert mechanical feedback on the biochemical events via deformation-dependent diffusion and inhibition. We show that active deformations can trigger chemomechanical bifurcations, yielding pulse spiral waves and global oscillations, which, with increasing mechanical feedback, give way to traveling or standing waves subsequently. Mechanical feedback is also found to contribute to stabilizing the polarity of emerging patterns, thus ensuring robust morphogenesis. Our results reproduce and unravel the experimentally observed solitary and multiple spiral patterns, which initiate asymmetric cleavage in *Xenopus* and starfish embryogenesis. This study underscores the crucial roles of mechanical feedback in cell development and also suggests a chemomechanical framework allowing for 3D large deformation and chemical signaling to explore complex morphogenesis in living shell-like structures.

active shell | chemomechanical coupling | morphodynamics | chiral pattern

Symmetry-breaking is a fundamental morphogenetic process in the development of organisms starting from their spherical zygotes to complex three-dimensional (3D) patterns and shapes, as widely observed in cell polarity establishment (1), cell protrusions (2, 3), and gastrula invagination (4, 5). Among these, left–right symmetry-breaking is one of the most basic and fascinating morphogenetic processes relevant to the biochemical and mechanical spiral pattern formation during early embryonic development (6, 7). Chemomechanical spiral patterns, which undergo continuous forming, oscillating, spreading, breaking, and vanishing, are also crucial to physiological processes. For example, the electric spiral wave in the heart is a sign of arrhythmia (8, 9), the Min-protein spiral waves in bacterial cells can control cell division site (10, 11), and spiral waves in the *Xenopus* cell cortex are related to chirality formation (12).

In the past decades, numerous asymmetric chemical patterns like spots, stripes, and spirals observed in biological structures have been explained based on Turing-like models (13, 14). However, typical biological morphogenesis involves tight integration of myriad biochemical signaling interactions with mechanical forces (15–18). It has been evidenced that self-organized chemical patterns on active soft materials can be triggered and strongly controlled by mechanical feedback (19–21), which is essential for physiological and pathological processes (22, 23). Recent chemomechanical models of active surfaces have considered mechanical factors including complex geometric deformation (24, 25), material flow (6, 26–28), curvature-sensitive membrane proteins (29–31), and deformation activation or inhibition on biochemical signals (32–35). These models can capture the axisymmetric patterns and deformations on deforming surfaces (25, 36), polar and nematic biochemical patterns on fixed surfaces (27), and 3D small undulations of active surfaces (30, 31). Yet, many bona fide morphogenetic processes involve asymmetric and large deformations, as spiral patterns experimentally observed in *Xenopus* embryos (Fig. 1A). On the other hand, as the most key hallmarks, the multichemical reactions and mechanical feedback emerge simultaneously in living structures but are often considered separately in previous theories, leaving the chemomechanical coupling unilateral (25, 37, 38). Therefore, a theoretical framework that couples direct mechanical feedback with chemical signaling pathways is highly desired to unveil the 3D patterning dynamics in soft living structures.

Significance

Biological morphogenesis involves rich symmetry-breaking events and orchestrated morphodynamics where chemical signaling and mechanical deformation are coupled. We propose a chemomechanical active elastic shell theory, which incorporates biochemical reaction–diffusion with mechanical feedback, to study the three-dimensional (3D) chiral pattern formation and evolution of the cell cortex. We show that the activity-driven chemomechanical bifurcations result in the formation of spiral waves, oscillations, traveling waves, and standing waves, accompanied by 3D large deformation. Our study demonstrates the significance of chemomechanical coupling in modulating pattern dynamics of cells and also provides a theoretical framework to explore 3D chemomechanical morphogenesis of other shell-like multicellular structures such as epithelial sheets, blastospheres, and organoids.

Author contributions: S.Y., B.L., and X.-Q.F. designed research; S.Y. performed theoretical modeling, linear stability analysis, and numerical simulations; S.Y., B.L., and X.-Q.F. wrote the paper.

The authors declare no competing interest.

This article is a PNAS Direct Submission.

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This article contains supporting information online at http://www.pnas.org/lookup/suppl/doi:10.1073/pnas.2206159119/-/DCSupplemental.

Published November 28, 2022.
In this study, we propose a chemomechanical theory to study the 3D large deformation and pattern dynamics of active viscoelastic shells in the elastic limiting, which can mimic a wide range of biological thin structures including the cell nuclei, cellular cortex, epithelial monolayers, and blastocysts. In particular, we focus on the formation, propagation, and transition of spiral waves in the cell cortex. The present theory incorporates active deformation under the regulation of biochemical signals such as RhoA and actomyosin, which exerts mechanical feedback on the biochemical reaction and diffusion. Linear stability analysis shows that the spontaneous formation of spiral and oscillatory patterns arises from the activity-driven chemomechanical bifurcations. Our numerical simulations further capture the dynamic pattern transitions to traveling or standing waves. We discover that mechanical feedback plays an important role in rectifying the polarity deviation induced by biochemical noises during pattern evolution. Our model characterizes the essential features of 3D chiral large deformation and pattern dynamics, which are forbidden in previous hydrodynamic models under axisymmetric constraints.

Results

Chemomechanical Active Shell Model. We account for the coupling of mechanical feedback and biochemical regulation in living active shells capable of 3D large deformations, such as the cell cortex. Fig. 1B illustrates a cell cortex that undergoes asymmetric deformation relevant to local chemical concentrations, as observed in the Xenopus embryo (Fig. 1A) (12). The active contraction in the cell cortex is generated via the motion of the actomyosin network, which is regulated by the upstreaming signal RhoA (Fig. 1C). In turn, the synthetic rate of RhoA can be inhibited by the actomyosin and active contraction upstreaming signal RhoA (Fig. 1D). The active contraction in the cell cortex is generated via the exchange factors (GEFs) (40). Therefore, we construct a simple three-component system composed of RhoA, actomyosin, and cortex contraction that shows the chemomechanical interplay.

![Fig. 1. Active shell model of a cell cortex. (A) A typical chemomechanical spiral pattern in the Xenopus embryo. Adapted from ref. 12 with permission. (B) Torsion deformation of the cell cortex induced by spiral chemical concentration. (C) The active contraction of the cell cortex stems from the motion of its actomyosin network, which is regulated by the activated RhoA concentration (i.e., activity). (D) A three-component feedback system composed of RhoA, actomyosin, and cortex contraction shows the chemomechanical interplay.](https://doi.org/10.1073/pnas.2206159119)

Active shell mechanics. Based on the Koiter shell theory (41), we model the cell cortex as an active viscoelastic shell of thickness \( h \). In general, the mechanical behavior of the cortex is dependent on the loading rate and the responding time. When the loads or stimuli are applied slowly, little elastic stress is stored in the cortex, and it behaves like a viscous fluid (25, 42). When the loads or stimuli are applied rapidly, however, the cortex does not have enough time to flow, and it stores stress at short timescales before the reorganization of the cortical network and the continuous turnover of F-actin and myosin (36, 43–45). We first deduce the mechanical governing equations of pure elasticity and then generalize the model to viscoelasticity with an effective temporal intermediate configuration (46–48). The mid-surfaces of this active shell in the initial, intermediate, and current configuration are \( \Gamma_0 \), \( \Gamma_t \), and \( \Gamma \), respectively. The corresponding first (second) fundamental forms are denoted as \( a_0 \) (\( b_0 \)), \( a \) (\( b \)), and \( a \) (\( b \)). The tangent plane of the mid-surface is spanned by the vectors \( e_\alpha \), and its normal vector is \( e_\nu \). Fundamental variables of this chemomechanical active shell are the displacement field \( \mathbf{u} = u^\alpha e_\alpha + u^\nu e_\nu \), RhoA activity \( \alpha_R \), and actomyosin activity \( \alpha_A \), with \( u^\alpha \) and \( u^\nu \) being displacements in the tangent plane and normal direction, respectively. Greek indexes take the values 1 and 2, and the subscripts ‘R’ and ‘A’ represent RhoA and actomyosin, respectively. According to the Kirchhoff–Love shell theory (49), the stretching and bending strains of the active shell are given as

\[
\varepsilon_{\alpha\beta} = \frac{1}{2} (a_{\alpha\beta} - \delta_{\alpha\beta}), \quad \kappa_{\alpha\beta} = b_{\alpha\beta} - \delta_{\alpha\beta}.
\]

The linear elastic strain energy density \( w_0 \) is

\[
w_0 = \frac{E \gamma^\alpha \gamma^\beta}{2(1-\nu^2)} \left( b_{\alpha\beta} \Gamma_{\gamma\delta} + \frac{\nu^3}{12} R_{\alpha\beta\Gamma} \right),
\]

with Young’s modulus \( E \), Poisson’s ratio \( \nu \), and the elastic tensor \( \gamma^\alpha \gamma^\beta = v^\alpha v^\beta \gamma^\delta + \frac{1}{2}(1+\nu)(\gamma^\gamma \gamma^\delta + \gamma^\delta \gamma^\gamma) \). Then, the membrane stresses and bending stresses are calculated as \( \sigma^{\alpha\beta} = \partial w_0 / \partial b_{\alpha\beta} \) and \( m^{\alpha\beta} = \partial w_0 / \partial \kappa_{\alpha\beta} \), respectively. Mechanical equilibrium equations are derived by the vanishing variation of the total potential energy \( \delta U_t = \delta U_c - \int_f f^{ext} \cdot \delta \mathbf{f} = 0 \), where the elastic strain energy \( U_c = \int_f w_0 d\Gamma \), the external force \( f^{ext} = f^\alpha e_\alpha + f^\nu e_\nu \), the virtual displacement of mid-surface is \( \delta \mathbf{r} \), and the area element \( d\Gamma = \sqrt{\gamma} dx^1 dx^2 \), with \( |\alpha| = \text{det}(a_{\alpha\beta}) \). The mechanical equilibrium equations of the deformed surfaces are given in Eq. 8 in Materials and Methods.

Biochemical Regulation. According to the non-Euclidean shell theory (38, 50), We could assume an intermediate mid-surface \( \Gamma^{Bio} \) of the cell cortex which is regulated by the spatiotemporal actomyosin activity through the isotropic stretch \( \Lambda(\alpha_A) \) and curvature deviation \( \kappa(\alpha_A) \) from its initial mid-surface \( \Gamma(24, 49, 50) \)

\[
\mathbf{a}^{Bio} = \Lambda^2(\alpha_A) \mathbf{a}_0, \quad \mathbf{b}^{Bio} = \Lambda(\alpha_A) \mathbf{b}_0 + \kappa(\alpha_A) \mathbf{a}_0.
\]

where

\[
\Lambda(\alpha_A) = \exp[-A_\Lambda(c_A - c^*_A)],
\]

\[
\kappa(\alpha_A) = -A_\kappa(c_A - c^*_A),
\]

with the asterisk denoting the quantities in the stationary state and the superscript “Bio” representing the biochemical regulations. These regulating functions, as shown in Fig. 2 A and B, capture both the intrinsic and extrinsic features of a deforming shell, complementary to the chemically controlled shell model developed previously (37).

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Viscoelasticity and elastic limit. The general viscoelastic active shell model could be derived by supplementing the evolving equation of the intermediate mid-surface, while the stresses remain the same form as those in the elastic model (46–48)

\[
\begin{align*}
\dot{\bar{a}} &= \dot{\bar{a}}^{\text{Bio}} + \frac{1}{\tau_v} (a - \bar{a}), \\
\dot{\bar{b}} &= \dot{\bar{b}}^{\text{Bio}} + \frac{1}{\tau_v} (b - \bar{b}),
\end{align*}
\]

where \(\tau_v\) is the viscous relaxation timescale. These governing equations show that the intermediate configuration of the viscoelastic active shell undergoes a continuous relaxation process that dissipates the activity-introduced energy. For a purely elastic active shell, i.e., \(\tau_v \to \infty\), the intermediate mid-surface is completely determined by biochemical activities without any dissipation, that is, \(\bar{a} = \bar{a}^{\text{Bio}}\) and \(\bar{b} = \bar{b}^{\text{Bio}}\).

The typical turnover time of F-actin and individual myosin is tens of seconds (51, 52), while the estimated viscous timescale of the embryonic cortex, which consists of cross-linked actomyosin networks, varies from 1 to 4 min roughly (53). It has been reported that the formation and persisting timescale of some chemomechanical patterns on the oocyte cortex is less than 1 min (54, 55). Without loss of generality, therefore, we first focus on the short-time limit of active shells as an elastic one and provide further simulation results of and discussion on the viscoelastic behaviors of active shells in SI Appendix.

Biochemical dynamics. We describe the two biochemical signaling dynamics based on a reaction–diffusion model incorporated with mechanical feedback

\[
\begin{align*}
\partial_t c_R &= D_R \Delta \Gamma c_R + f(c_R, c_A) - k_M \varphi(u), \\
\partial_t c_A &= D_A \Delta \Gamma c_A + g(c_R, c_A),
\end{align*}
\]

where \(D_R\) and \(D_A\) are the diffusion coefficients of two bio-chemicals, and \(\varphi(u)\) is the direct mechanical feedback function with strength \(k_M\). \(\Delta \Gamma(\cdot) = (1/\sqrt{|a|}) \partial_{\alpha} [a^{\beta} \sqrt{|a|} \partial_{\beta}(\cdot)]\) is the Laplace–Beltrami operator on the deformed surface \(\Gamma\), which involves the indirect regulation of mechanical deformation on biochemical dynamics. Considering the active shell as an excitable medium with fast triggering variable \(c_R\) and slow recovery variable \(c_A\), the chemical reaction functions are assumed in the forms of modified FitzHugh–Nagumo (FHN) equations as

\[
\begin{align*}
f(c_R, c_A) &= k_{on} + k_R (c_1 - c_R)^2 (c_2 - c_R) - k_A c_A, \\
g(c_R, c_A) &= \varepsilon (c_R - \beta c_A - \beta_0),
\end{align*}
\]

with fixed parameters \(k_{on}, k_R, c_1, c_2, \varepsilon, \beta, \beta_0\) (56, 57). In our calculations, all physical quantities are rescaled by the characteristic length \(\ell\) and characteristic time \(\tau = R_0^2/D_R\). The dimensionless parameters, denoted by a tilde, are given in Materials and Methods.

Mechanical feedback. In general, the mechanical feedback function \(\varphi(u)\) is dependent on the 3D elastic deformations of the shell. For simplicity, we assume that the function is related only to the mean curvature \(H = \text{tr}(b)/2\) (29, 33, 58, 59), because bending is in general dominant in the deformation of thin shells. The Laplacian of mean curvature can, to some extent, represent the curvature-driven force in analogy with the temperature-driven heat flux. We then adopt a sigmoid function of the relative mean curvature to ensure the mechanical feedback in an appropriate regime (Fig. 2C)

\[
\varphi(u) = \varphi(H) = \frac{2}{1 + \exp[k_H \Delta \Gamma (H/H^* - 1)]} - 1,
\]

where \(H^*\) is the mean curvature of the stationary shell. Altogether, Eqs. 1–6 represent a minimal model for the chemomechanical active shell capable of 3D large deformations, where chemical signal regulations, active deformations, and direct mechanical feedback are embraced.

Chemomechanical instability. We perform the linear stability analysis of the stationary state in an initially spherical shell of radius \(R_0\). Under the osmotic pressure \(\Delta P\), the radius of the stationary elastic shell becomes \(R^*\), and the homogeneous concentration fields are \(c_I = c^*_I\) (\(I = R, A\)). Linearizing the
governing equations via expanding variables fields to the first order of small perturbations in the forms of scalar (vectorial)
spherical harmonics $Y_{lm}(Y_{lm})$, we obtain the characteristic
equation $\delta \delta \delta \delta = J(\delta \delta \delta \delta) \delta \delta \delta \delta$. The eigenvalue $\xi_l$ of Jacobian matrix $J$ is the growth rate of the $l$-th eigenmode, where the
positive real part of $\xi_l$ denotes an unstable stationary state (SI Appendix
details).

With neither diffusion nor mechanical feedback, the purely
chemical system degenerates to a classical FHN model which can exhibit excitabile, oscillatory, and stable states with low,
intermediate, and high can exhibit excitable, oscillatory, and stable states with low,
for details). For excitable states with low $c_R$, the stationary state is locally
stable near the equilibrium ($\xi_l < 0$), as shown in Fig. 3A, but globally unstable when the perturbation exceeds a threshold,
then initiating a large excursion along the left and right arms of the $N$-shaped nullcline (SI Appendix, Fig. S1A) (60). For a
reaction–diffusion system on a spherical surface, this excitabile
kinetics will trigger a pulsatory spiral wave, as shown in region
(I) in Fig. 3C. Sufficient spatial diffusion can lead to a local
excitation, where the neighboring resting state region is switched
to the excited one, forming a wavefront. This wavefront then
undergoes a slow recovery transition, called refractory, back to
the resting state and generates the wave back. Since the time
spent in the refractory process is much longer than the time
for excitation, the wave back and front will never touch each other (61), giving rise to a pulsatory spiral wave in the spherical
shell. For the excitabile state with both diffusion and mechanical
deforations, increasing negative mechanical feedback may turn
the largest real part of the growth rate positive at $l \geq 1$ due to the
pitchfork bifurcation (Fig. 3A and SI Appendix, Fig. S2),
resulting in traveling waves [see region (III) in Fig. 3C]. In
contrast, the positive mechanical feedback keeps the growth rate
negative for all modes, thus maintaining the system excitabile
(Fig. 3A).

When the stationary RhoA activity $\rho^*_R$ increases to an
intermediate value, the purely chemical system undergoes a
pitchfork bifurcation ($\xi_l |_{l=0} > 0$, Fig. 3B), which, interestingly,
can generate a relaxation oscillation (Fig. 3D). This oscillation,
differing from the generic Hopf bifurcation-induced simple
harmonic oscillation (62), stems from the mismatch of time
scales of the fast triggering variable $c_R$ and the slow recovery
variable $c_A$. The scaling analysis shows the oscillation period
$T \sim \tilde{\xi}_{0.88}^{-1}$ (Fig. 3E). With spatial diffusion, any initial chemical
perturbations on the shell will vanish, and global relaxation
oscillations will soon occur in the chemical system, as shown
in region (II) in Fig. 3C and Movie S3. With increasing negative
mechanical feedback, this global unstable stationary state ($l = 0$)
arrives at a finite-wavelength instability $l > 1$ as shown in
Fig. 3B and SI Appendix, Fig. S2, exhibiting traveling or standing
wave patterns (see region (III) in Fig. 3C, SI Appendix, Fig. S3
and Movie S4). The standing waves accompanied by shape
oscillations also emerge when the initial RhoA is concentrated
on both the north and the south pole (SI Appendix, Fig. S4).
Together, the chemomechanical morphodynamics depends on
the competition between the chemical and mechanical instability,
which favors global oscillations and finite-wavelength instability,
respectively.

3D Asymmetric Morphodynamics of Active Shells. To capture
the nonlinear dynamics beyond the stationary state, we develop
a numerical method based on the double Fourier sphere (DFS)
method (63). We track 3D large deformations and chemical
concentrations far from the stationary state.

Soliditary spiral and traveling waves. We first investigate the
symmetry-breaking processes of active shells under the chemome-
chanical coupling regulation, which reproduces the asymmetric
cleavage processes in Xenopus (12). The simulation parameters

![Fig. 3. Growth rate as a function of the mode number $l$ for different stationary RhoA activities (A) $c^*_R = 0.15$ and (B) $c^*_R = 0.5$. Colored solid lines represent the real part of the largest growth rate, and dashed lines represent the complex part. (C) Phase diagram as a function of stationary RhoA activity $c_R$ and dimensionless strength of negative mechanical feedback $\kappa_M$, which is obtained from linear stability analysis. Four regions including (I) pulsatory spiral wave (pink), (II) global relaxation oscillation (orange), (III) traveling and standing waves (blue), and (IV) stable region (white) can be distinguished. The red lines represent a chemical-induced pitchfork bifurcation, while the blue lines represent the mechanical feedback-induced pitchfork bifurcation. The insets show numerical simulations of the evolution of these patterns on deforming shells. Initial conditions are assumed as locally concentrated RhoA near the north pole. Parameters used in the simulations are $\kappa_R = 0.15$, $\kappa_M = 0.1$; (II) $c^*_R = 0.5$, $\kappa_M = 0$; (III) $c^*_R = 0.15$, $\kappa_M = 0.2$ (traveling wave) and $c^*_R = 0.5$, $\kappa_M = 5$ (standing wave); (IV) $c^*_R = 0.8$, $\kappa_M = 0$. (D) RhoA and actomyosin concentrations change with time when global oscillation occurs. Parameters are $c^*_R = 0.5$, $\kappa_M = 0$, and $\tilde{\xi} = 0.02$. (E) The oscillation period $T$ as a function of the parameter $\tilde{\xi}$, showing the scaling law $T \sim \tilde{\xi}_{0.88}$.](https://doi.org/10.1073/pnas.2206159119)
are chosen in the spiral wave and traveling wave domain [regions (I) and (III)] in the phase diagram, where \( \sigma_R \) is concentrated in the spherical cap domain deviated \( \theta_0 = \pi / 3 \) from the north pole and declining otherwise in the form of a Gaussian function (SI Appendix), and \( \sigma_A \) is assumed to be concentrated in a cap near the north pole. This initial chemical distribution indicates a small perturbation in the biological genetic guidance, which should be parallel to the animal–vegetal (A–V) axis (32). In biological systems, white noises and initial imperfections of biochemicals are both common, but, for simplicity, we here consider only the latter (SI Appendix for details). With shape changes and relatively weak mechanical feedback (Fig. 4A), a solitary pulse spiral wave accompanied by chiral elastic deformation is first triggered and then wanders around the whole shell. When it passes the north pole the second time, the former spiral wave breaks into two reverse spiral waves and then undergoes sequential merging, breaking, and annihilation (Movie S1). In the meantime, the spherical shell shows a nematic deformation, whose axis deviates from the A–V axis. This can explain asymmetric cell polarization and cell division observed in experiments, such as polarized cleavage with spiral biochemical waves in Xenopus (12).

Furthermore, we examine the 3D morphodynamics of the active shell under stronger negative mechanical feedback with the same initial conditions (Fig. 4B). Similarly, the mechanical instability-induced chemical traveling waves undergo forming, breaking, and vanishing, along with the asymmetric 3D large deformations on the elastic shell (Movie S2). This traveling pattern resembles the spherical harmonic function with \( l = 4 \), \( m = 0 \), which agrees with the linear stability analysis in Fig. 3d. Despite the initial chemical perturbations being slightly deviated from the A–V axis, the traveling waves show a quick recovery and rectifying behavior that helps to define the nematic axis. This correction on the nematic axis is completely spontaneous without any presumed nematic signals or geometries, which is different from the prescribed cues introduced in ref. 27. Thus, our theory captures the effect of mechanical feedback on the robust asymmetric morphogenesis processes. Moreover, we investigate the viscoelastic effect on the formations and transitions of solitary spiral waves. Our numerical simulations show that if the viscosity is strong enough, the mechanical feedback will not lead to pattern transitions from spiral to traveling waves. Detailed discussions on 3D morphological evolution with different viscous timescales \( \tau_V \) are provided in SI Appendix, section 4 and Fig. S6.

Biochemical signaling patterns have been proven to play an important role in cell division, proliferation, polarization, and migration, which are ubiquitous in biological processes from embryogenesis to tissue morphogenesis. The module “RhoA-actomyosin-cortex deformation” we have proposed above can be the down-streaming effector of many key signaling pathways. For cell division, the RhoA and actomyosin dynamics are triggered by the gradient of upstreaming APC/C-Cdk1-cyclinB signaling pathway as well as Rho GEF (Ect2), which regulates the cell cycle and cytokinesis in starfish oocytes and embryos (39). The emerging self-organized traveling waves of enzymatic activities can ensure the synchronization of cell division processes across large embryos. For cell polarity and migration, spontaneous actin polymerization waves can generate cell motion, polarization, and migration. For example, spiral actin waves can exert forces on the cell membrane and contribute to cell movement and polarization. The generation of these actin polymerization waves is dependent on Arp2/3, and the wave propagation is altered by ROCK (64). Cell signaling, such as PIP3, Rac1, Arp2/3, cofilin, and shootin1, has also been discovered to regulate axonal actin waves and therefore affect axon outgrowth, branching, and polarity formation (65).

**Multispiral waves.** We have elucidated the mechanisms for the formation of a single solitary spiral wave, a kind of trigger waves, and its transition to traveling and standing waves on the chemomechanical active shell. However, recent experiments evidenced that multispiral waves may emerge on living active shells (13, 54, 55). As shown in Fig. 5A, coordinated RhoA turbulent spiral waves and 3D large deformations arise on the starfish oocytes simultaneously (55). To further challenge our chemomechanical active shell theory, we simulate this dynamic process by introducing several random defects in chemical fields as initial conditions (SI Appendix).

Our simulation shows that the 3D chemomechanical chiral patterns observed in starfish oocytes can be well reproduced (Fig. 5B), revealing the robustness of the proposed theory. Remarkably, left-hand and right-hand spirals can form randomly and persistently merge and annihilate when they meet. Meanwhile, new small spirals spring up in the central region and then travel outward, during which they are connected and form a

![Fig. 4](https://doi.org/10.1073/pnas.2206159119)

**Fig. 4.** 3D large deformation of the active elastic shell under the regulation of biochemical and mechanical interplay with negative mechanical feedback strength (A) \( \tilde{k}_M = 0.1 \) and (B) \( \tilde{k}_M = 0.2 \). In (B), solitary spiral waves can transit to traveling waves. The upper rows in each panel represent RhoA activity \( c_R \) in the intact deforming shell, the middle rows show the front and back of spiral and traveling waves, and the bottom rows represent the normal displacement \( u^\nu \).
large ring around the shell. These chemical spirals stem from the interaction of solitary trigger waves, distinct from the phase waves simulated in a pure reaction–diffusion system based on the complex Ginzburg–Landau equation (54, 55). Generally, the speed of phase waves is infinite, while the speed of trigger waves is finite and controlled by the diffusion coefficients and the time scales of fast and slow variables.

In addition, these results also suggest that solitary spiral waves can serve as a fundamental component for yielding complex 3D chiral morphodynamics through superposition. Previous experimental and theoretical work has focused on the dynamics of topological turbulence, where the complex Ginzburg–Landau continuum model and Helmholtz–Onsager point vortex model were adopted in analogy with quantum physics (54, 55). Although those simulation results are phenomenologically similar to the experimental observations, many parameters involved hardly find corresponding measurable biological quantities or variables. Furthermore, these two studies aimed to describe and capture the turbulent dynamics of biochemical signaling rather than elucidating the mechanisms underlying the formation of biochemical spiral waves and the mechanical deformation entangled with them. Actually, mechanical deformations like the surface contraction waves have been reported previously (32, 39, 66) and proved to be not only tightly related to but have feedback on the biochemical dynamic patterns (67). Here, our model encompasses both the biochemical diffusing on the continuously deforming shells and their synthetic and decomposing rates affected by the stress state or the local curvature, which could help to deeply understand the dynamics of complex biochemical patterns accompanied by large deformations.

Discussion

We have studied the dynamics of self-organized chemical waves and 3D large deformations in active viscoelastic shells. We identified the global instability and local pitchfork bifurcation mechanism underlying the spontaneous symmetry-breaking patterns including spiral waves, traveling waves, and standing waves, and global relaxation oscillations. This morphodynamics is modulated by the interactions of biochemical reactions, diffusion, and mechanical feedback. Our results can reproduce and explain the synchronized chiral deformations and complex chemical patterning observed in cell cortices such as Xenopus embryos and starfish oocytes. Our study also highlights the significance of mechanical feedback levels in modulating pattern dynamics and suggests that appropriate mechanical feedback on biochemicals can be even harnessed to suppress abnormal spiral waves, which often emerge in the human cerebral cortex and heart and have lethal outcomes when uncontrolled (9, 68). In addition, occasionally misexpressed spatiotemporal biochemicals may deviate the nematic axis from the polar axis in cell development, while strong enough mechanical feedback can correct the deviated axis back and stabilize the polarity reliably. It further reveals the crucial role of the mechanical feedback mechanism in ensuring robust morphogenesis.

Our active viscoelastic shell presents a minimal model for deciphering the morphodynamics of living biological shells. However, it captures the most essential features including the biochemical reaction and regulation, active deformations, and mechanical feedback in a short-time elastic limit. Further studies need to consider remodeling (69), more complex constitutive relations like nonlinear elasticity (70), cortex rheology (43), and the stimuli and forces from the environment, e.g., the interactions from cytoplasm on the cellular cortex (27). We expect that more in vitro and in vivo experiments could validate our theory in different aspects, for example, the biochemical reactions using genetic techniques such as the gene knockdown, the local stress distribution using the force inference method, and the 3D morphological evolution by light sheet microscopy. The proposed chemomechanical model can be easily extended to other complex biological systems such as multicellular embryos and blastospheres and to reveal more substantial mechanisms of self-organization and 3D symmetry-breaking during biological development.

Materials and Methods

Mechanical Equilibrium. The membrane stresses and bending stresses are calculated as

$$\sigma_{\alpha\beta} = \frac{E_h}{1 - \nu^2} A_{\alpha\beta\gamma\delta} \delta_{\gamma\delta} G_{\nu\delta}, \quad m_{\alpha\beta} = \frac{E_h^3}{12(1 - \nu^2)} A_{\alpha\beta\gamma\delta} B_{\gamma\delta}. \quad [7]$$

The mechanical equilibrium equations of the normal force $f^n$ and the in-plane forces $f^\alpha$ are given as

$$f^n = \frac{1}{\sqrt{|a|}} \frac{\partial}{\partial x^\alpha} \left[ \frac{\partial}{\partial x^\alpha} \left( \sqrt{|a|} m_{\alpha\beta}^\mu \right) + \sqrt{|a|} \Gamma^\alpha_{\beta\delta} m_{\delta\beta}^\mu \right]$$

$$f^\alpha = \frac{1}{\sqrt{|a|}} \frac{\partial}{\partial x^\alpha} \left[ \sqrt{|a|} (\sigma_{\alpha\beta} + m_{\beta\gamma} b_{\mu\gamma} (a^{-1})^\gamma^\alpha) \right] + \Gamma^\alpha_{\beta\delta} \left( \sigma_{\delta\beta} + m_{\beta\gamma} b_{\mu\gamma} (a^{-1})^\gamma^\delta \right) + \left( \frac{1}{\sqrt{|a|}} \frac{\partial}{\partial x^\alpha} \left( \sqrt{|a|} m_{\alpha\beta}^\gamma \right) + \Gamma^\alpha_{\beta\delta} m_{\delta\beta}^\gamma \right) b_{\mu\lambda} (a^{-1})^\lambda^\alpha,$$

and the stress boundary conditions read

$$n_{a} m_{\alpha\beta}^a m_{\gamma\delta} = 0,$$

$$n_{\beta} \left[ \sigma_{\alpha\beta} + (a^{-1})^\gamma^\alpha b_{\mu\gamma} m_{\beta\gamma} \right] = 0,$$

$$n_{\alpha} \left[ \sigma_{\alpha\beta} (\sqrt{|a|} m_{\alpha\beta}^\gamma) + \sqrt{|a|} \Gamma^\alpha_{\beta\gamma} m_{\gamma\delta} b_{\mu\lambda} (a^{-1})^\lambda^\gamma \right] = 0,$$

where $(x^1, x^2)$ are the curvilinear coordinates, $\Gamma^\gamma_{\alpha\beta}$ are the second Christoffel symbols, and the metric tensor satisfies $(a^{-1})^\alpha^\gamma b_{\mu\gamma} m_{\beta\gamma} = \delta_{\beta}^\gamma$. If the active shell is suspended in a fluid environment which provides frictional damping, the external forces can be calculated as $f^{ext} = \eta u$ with $\eta$ being the friction coefficient of the surrounding fluid.
Deformation are normalized as the reaction–diffusion equations of biochemical signals coupled to mechanical characteristic time diffusivity ratio. Diffusion of RhoA and actomyosin are both considered in the dynamics, where themselves autocatalytically, while actomyosin is considered an inhibitor. We adopt the modified FHN equation to capture its excitability. RhoA is a good candidate for the activator as small GTPases and can indirectly activate mechanical feedback. Nondimensional Chemical Dynamics.

| Parameter | Value | Physical meaning |
|-----------|-------|------------------|
| $a_1$ | 0.25 | Parameter in FHN equations |
| $a_2$ | 1 | Parameter in FHN equations |
| $a_0$ | 0–1 | RhoA synthetic rate |
| $\rho_0$ | 0.1 | Actomyosin degradation rate |
| $\beta$ | 1 | Actomyosin self-inhibition rate |
| $\varepsilon$ | 0.01 | RhoA activation on actomyosin |
| $D$ | 0.1 | Relative diffusivity of actomyosin |
| $k_R$ | 8 | RhoA self-activation rate |
| $k_A$ | 1.5 | Actomyosin inhibition on RhoA |
| $h$ | 0.15 | Shell thickness |

Numerical Methods. In the simulations, we consider the diffusion and reaction with mechanical feedback of chemical signals on a constantly deforming shell. The simultaneously changing chemical and mechanical fields are solved through a double-Fourier spherical (DFS) method. At each time $t$, we solve the mechanical equilibrium Eq. 8 via an implicit iteration method, obtaining the displacement fields under the regulation of current chemical concentrations. Since the normal displacement is dominant, i.e., $|u^N| > |u^p|$, we can neglect the in-plane displacements in the equilibrium equations. Therefore, only normal equilibrium equations should be solved with one variable $u^N$; while the in-plane equilibrium equations are not strictly satisfied. In this way, we do not need to assume that the chemical concentrations are near the stationary state like [25], or the chemical regulations in Eq. 3 leave only the modulation on curvature while the modulation on stretching vanishes ($\Delta (A_R) = 1$) in previous curvature-sensitive models (29, 31, 71). After obtaining the displacement fields $u^N$ at $t$, we can solve the nondimensional chemical dynamic Eq. 10 in the deforming configuration through a fourth-order, sixth-stage, linearly semi-implicit Runge-Kutta method (63).

Data, Materials, and Software Availability. All study data are included in the article and/or SI Appendix.

Acknowledgments. Supports from the National Natural Science Foundation of China (grants 12032014, 11921002, 11922207, and 11961131005) are acknowledged.

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