ELECTRONIC SUPPLEMENTARY INFORMATION FOR

Influence of myosin activity and mechanical impact on keratocyte polarization

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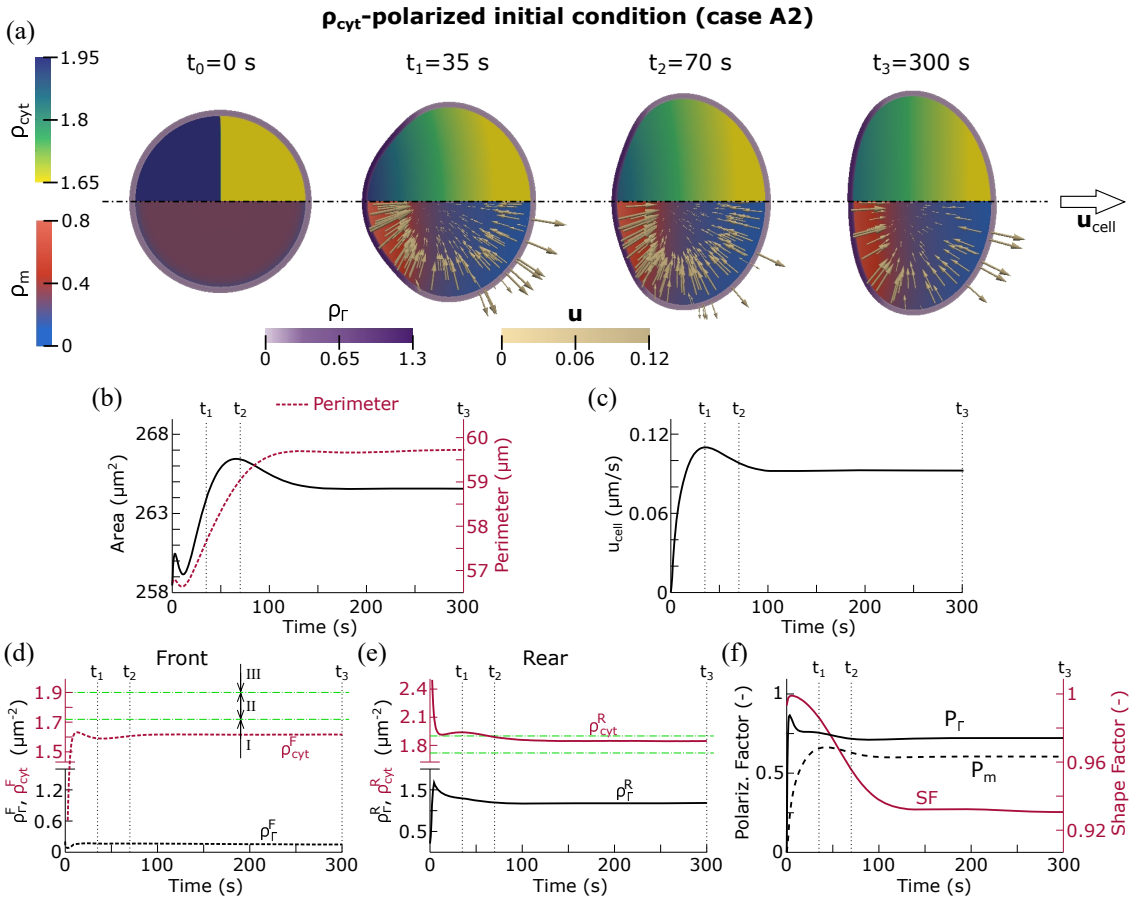

Fig. S1 Model results of a keratocyte with a non-uniform ρ_{cyt} distribution as initial condition (case A2). The rest of the unknowns exhibit a uniform distribution at the initial time. *(a)* ρ_Γ distribution on the membrane and ρ_{cyt} (top half of the cell) and ρ_m (bottom half of the cell) distributions on the cytosol at times $t_0 = 0$, $t_1 = 35$, $t_2 = 70$, and $t_3 = 300\,\text{s}$. Arrows in the bottom half represent the velocity field $\boldsymbol{u}$. The dash-dotted line represents the axis of symmetry of the cell traced by the cell's center of mass. The cytosolic distributions are symmetric with respect to the axis of symmetry. Time evolution of *(b)* the cell area (black solid line) and perimeter (red dashed line); *(c)* the velocity of the cell's center of mass u_{cell}; *(d)* ρ_{cyt} and ρ_Γ at the front edge of the cell at the axis of symmetry, denoted as ρ^F_{cyt} (red dashed line) and ρ^F_Γ (black dashed line), respectively; *(e)* ρ_{cyt} and ρ_Γ at the rear edge of the cell at the axis of symmetry, denoted as ρ^R_{cyt} (red solid line) and ρ^R_Γ (black solid line), respectively; and *(f)* cellular shape factor (SF, red solid line) and polarization factors P_Γ (black solid line) and P_m (black dashed line). Vertical dotted lines in the graphs indicate the times t_1, t_2, and t_3. The horizontal green dash-dotted lines in *(d)* and *(e)* represent the densities ρ^I_{cyt} and ρ^{II}_{cyt}, which separate regions I and II, and II and III, respectively, in the f_ρ diagram (see Fig. 2 in the main text).

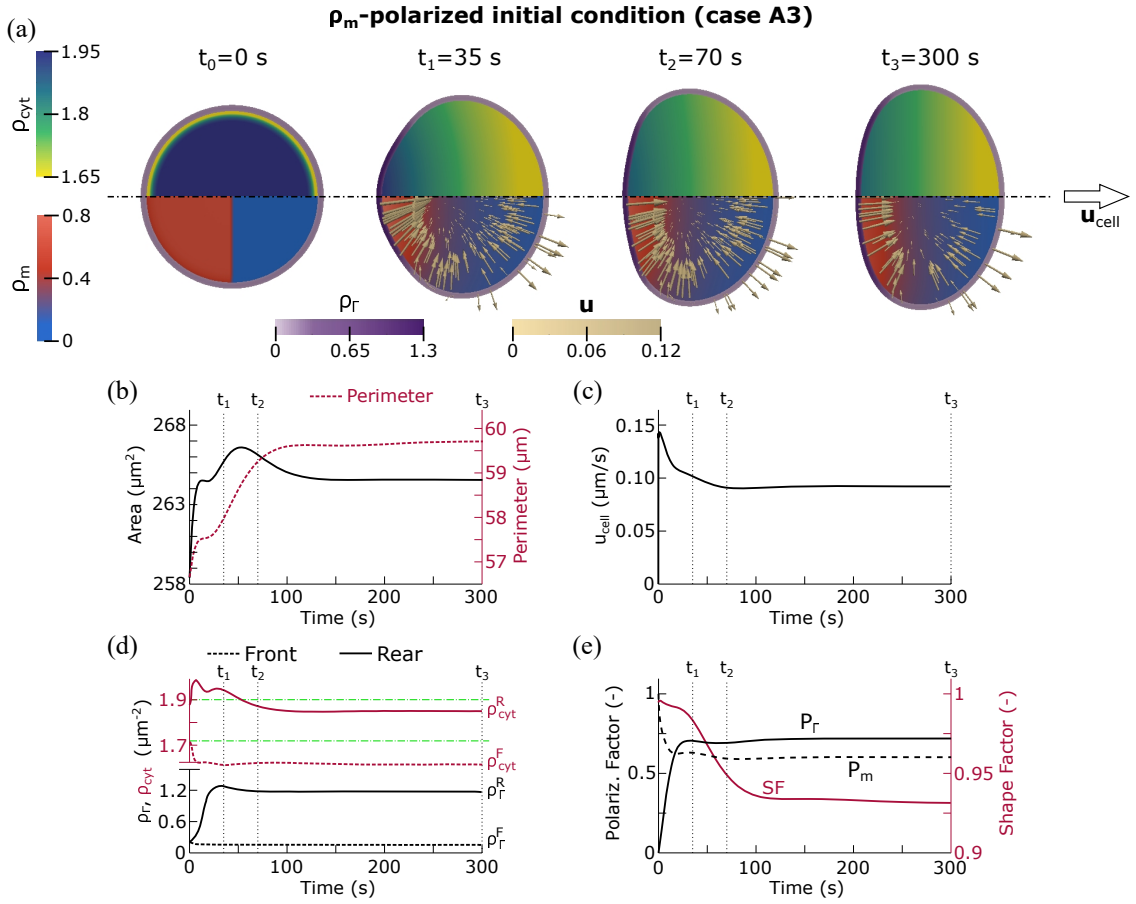

Fig. S2 Model results of a keratocyte with a non-uniform ρ_m distribution as initial condition (case A3). The rest of the unknowns exhibit a uniform distribution at the initial time. The layout of the figure is analogous to Fig. S1. *(a)* ρ_Γ, ρ_{cyt}, ρ_m and $\boldsymbol{u}$ distributions at four different times. Time evolution of *(b)* cell area and perimeter; *(c)* u_{cell}; *(d)* ρ^F_{cyt}, ρ^F_Γ, ρ^R_{cyt}, and ρ^R_Γ; and *(e)* cellular shape factor (SF), P_Γ, and P_m.

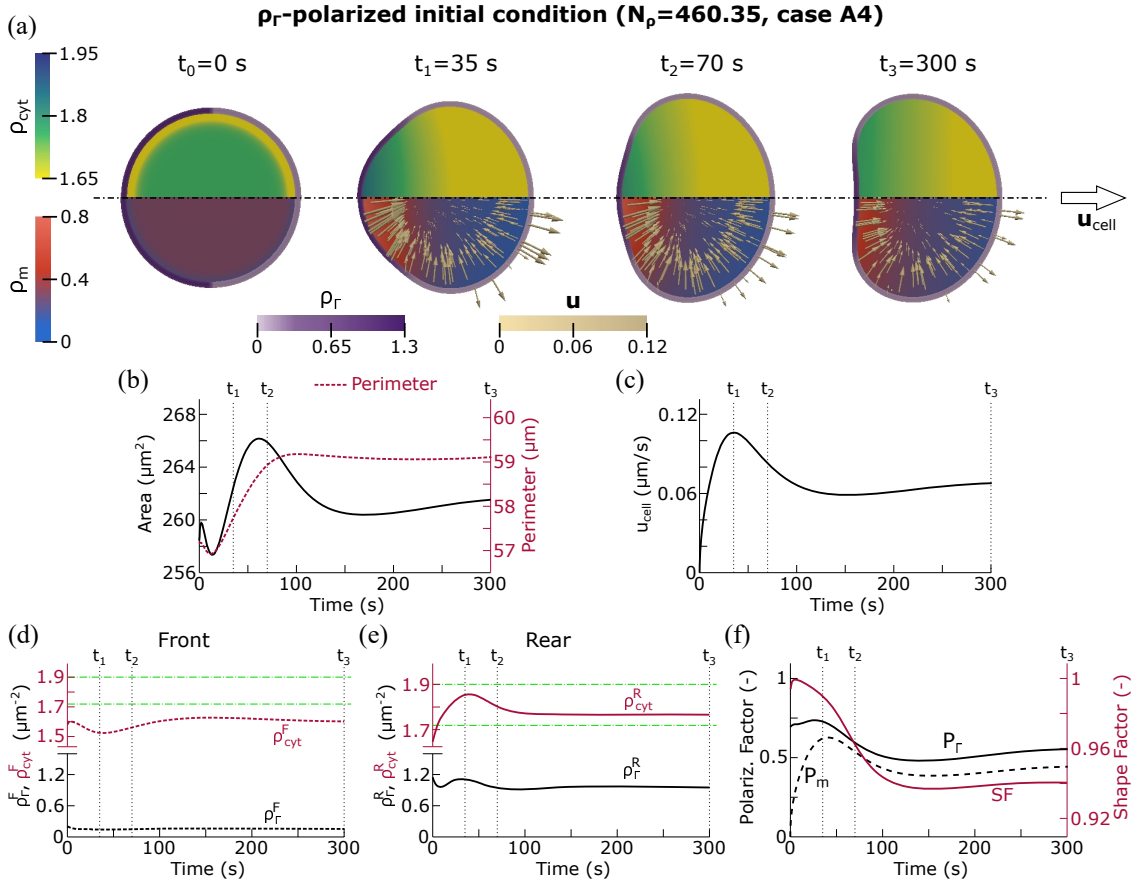

Fig. S3 Model results of a keratocyte with a non-uniform ρ_Γ distribution as initial condition and a total amount of RhoA proteins $N_\rho = 460.35$ (case A4). The rest of the unknowns exhibit a uniform distribution at the initial time. Note that $N_\rho = 488.9$ in the rest of the cases shown in the paper. The layout of the figure is identical to Fig. S1. The cell achieves a polarized and motile steady state, which is slightly different from the steady state of cells with $N_\rho = 488.9$; compare with Fig. 4 (case A1) in the main text.

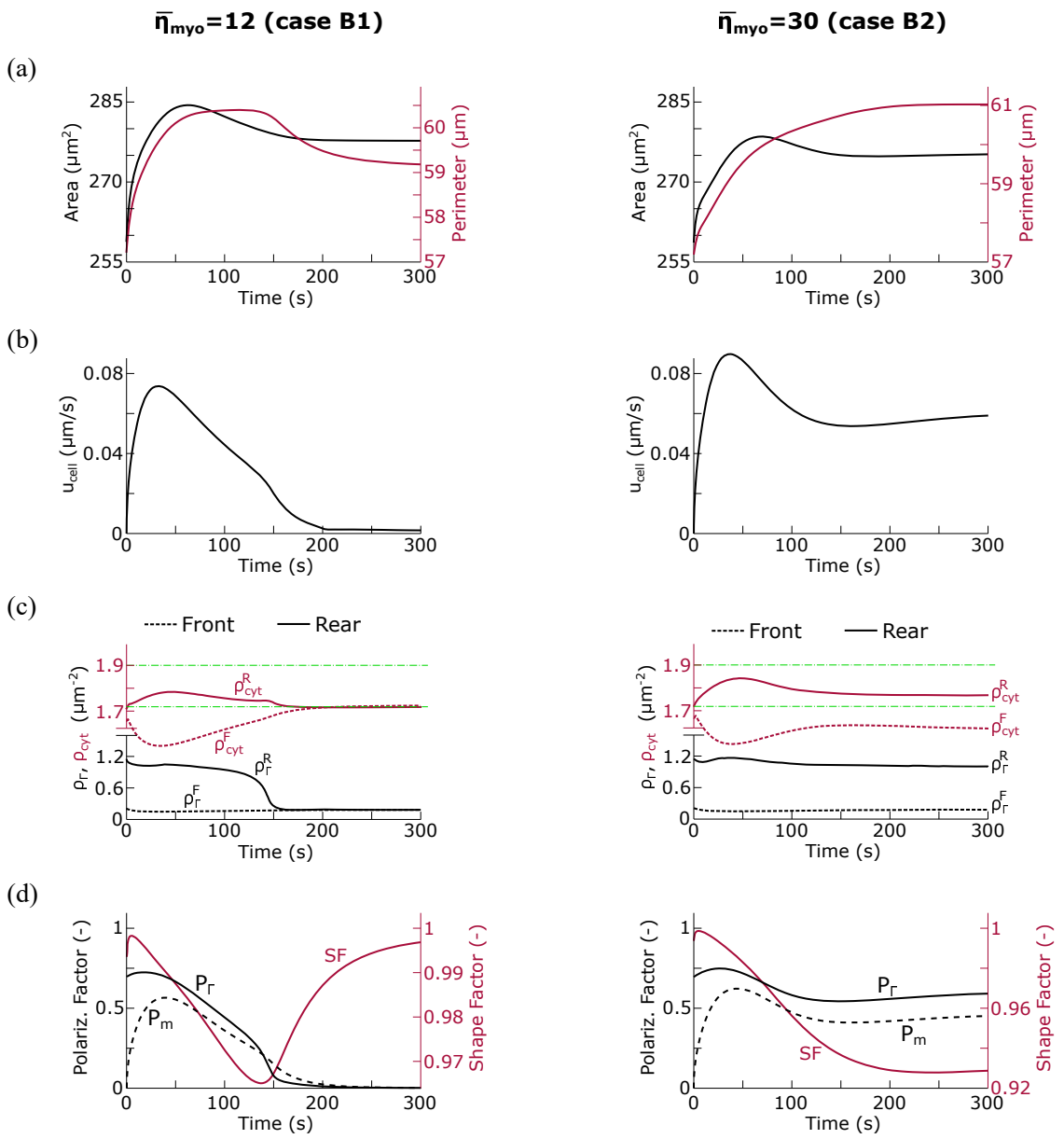

Fig. S4 Comparison between cells with different levels of myosin inhibition. On the left column, results corresponding to $\overline{\eta}_{\mathrm{myo}} = 12\,\mathrm{pN}\mu\mathrm{m}$ (case B1). On right column, results corresponding $\overline{\eta}_{\mathrm{myo}} = 30\,\mathrm{pN}\mu\mathrm{m}$ (case B2). The layout of the figure is analogous to subpanels (b)–(f) in Fig. S1. Time evolution of *(a)* cell area and perimeter; *(b)* u_{cell}; *(c)* ρ^F_{cyt}, ρ^F_Γ, ρ^R_{cyt}, and ρ^R_Γ; and *(d)* SF, P_Γ, and P_m. High levels of myosin inhibition (left column) impede the attainment of a steady polarized state, while low levels of myosin inhibition (right column) allow for cell polarization and motion.

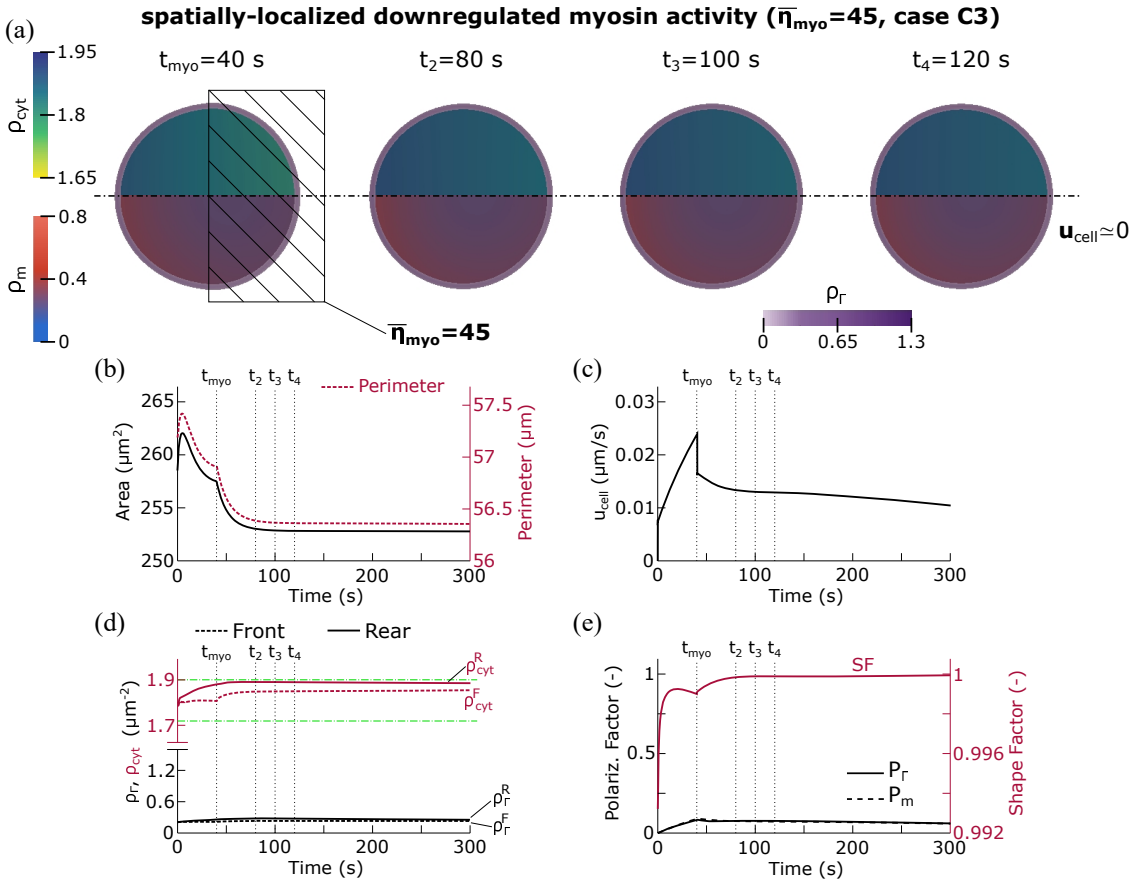

Fig. S5 Spatially-localized downregulation of myosin activity (case C3). Model results of a keratocyte with a non-polarized initial condition (see, e.g., t_0 in Fig. 3(a) in the main text). Myosin activity is reduced such that $\overline{\eta}_{\rm myo} = 45\,{\rm pN}\mu{\rm m}$ in the front half of the cell for $t < t_{\rm myo} = 40\,{\rm s}$. Otherwise, $\overline{\eta}_{\rm myo} = 60\,{\rm pN}\mu{\rm m}$. The layout of the figure is analogous to Fig. S1. *(a)* ρ_Γ, $\rho_{\rm cyt}$, and ρ_m distributions at four different times. Myosin activity is downregulated in the striped region (front half of the cell). Time evolution of *(b)* cell area and perimeter; *(c)* $u_{\rm cell}$; *(d)* $\rho^F_{\rm cyt}$, ρ^F_Γ, $\rho^R_{\rm cyt}$, and ρ^R_Γ; and *(e)* SF, P_Γ, and P_m. The sharp transition of the plots at $t_{\rm myo}$ is due to the sudden change of $\overline{\eta}_{\rm myo}$, which recovers its standard value ($\overline{\eta}_{\rm myo} = 60\,{\rm pN}\mu{\rm m}$). The cell is unable to attain a steady polarized state. A higher level of myosin downregulation is required to achieve a polarized and motile steady state (see Fig. 7 in the main text).

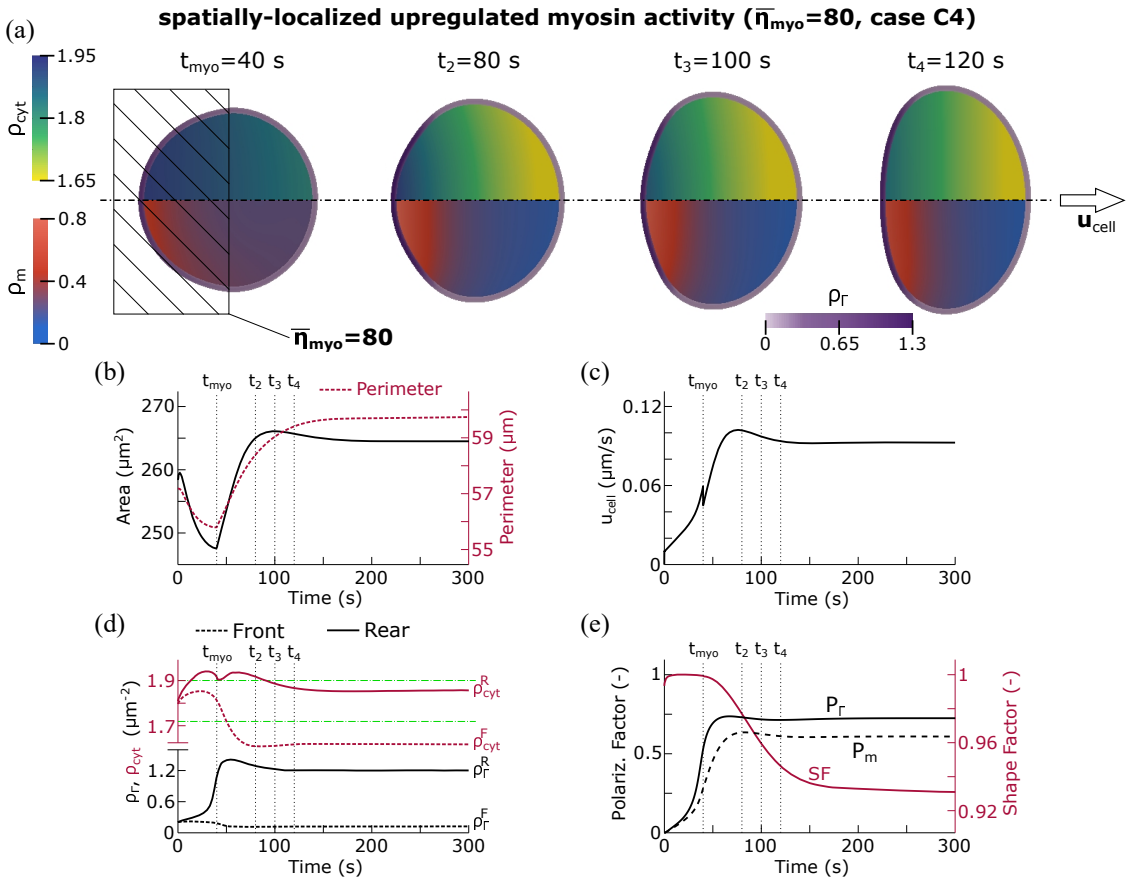

Fig. S6 Spatially-localized upregulation of myosin activity (case C4). Model results of a keratocyte with a non-polarized initial condition (see, e.g., t_0 in Fig. 3(a) in the main text). Myosin activity is increased such that $\overline{\eta}_{\rm myo} = 80\,{\rm pN}\mu{\rm m}$ in the rear half of the cell for $t < t_{\rm myo} = 40\,{\rm s}$. Otherwise, $\overline{\eta}_{\rm myo} = 60\,{\rm pN}\mu{\rm m}$. The layout of the figure is identical to Fig. S5. *(a)* ρ_Γ, $\rho_{\rm cyt}$, and ρ_m distributions at four different times. Myosin activity is upregulated in the striped region (rear half of the cell). Time evolution of *(b)* cell area and perimeter; *(c)* $u_{\rm cell}$; *(d)* $\rho^F_{\rm cyt}$, ρ^F_Γ, $\rho^R_{\rm cyt}$, and ρ^R_Γ; and *(e)* SF, P_Γ, and P_m. The cell achieves a steady polarized state.

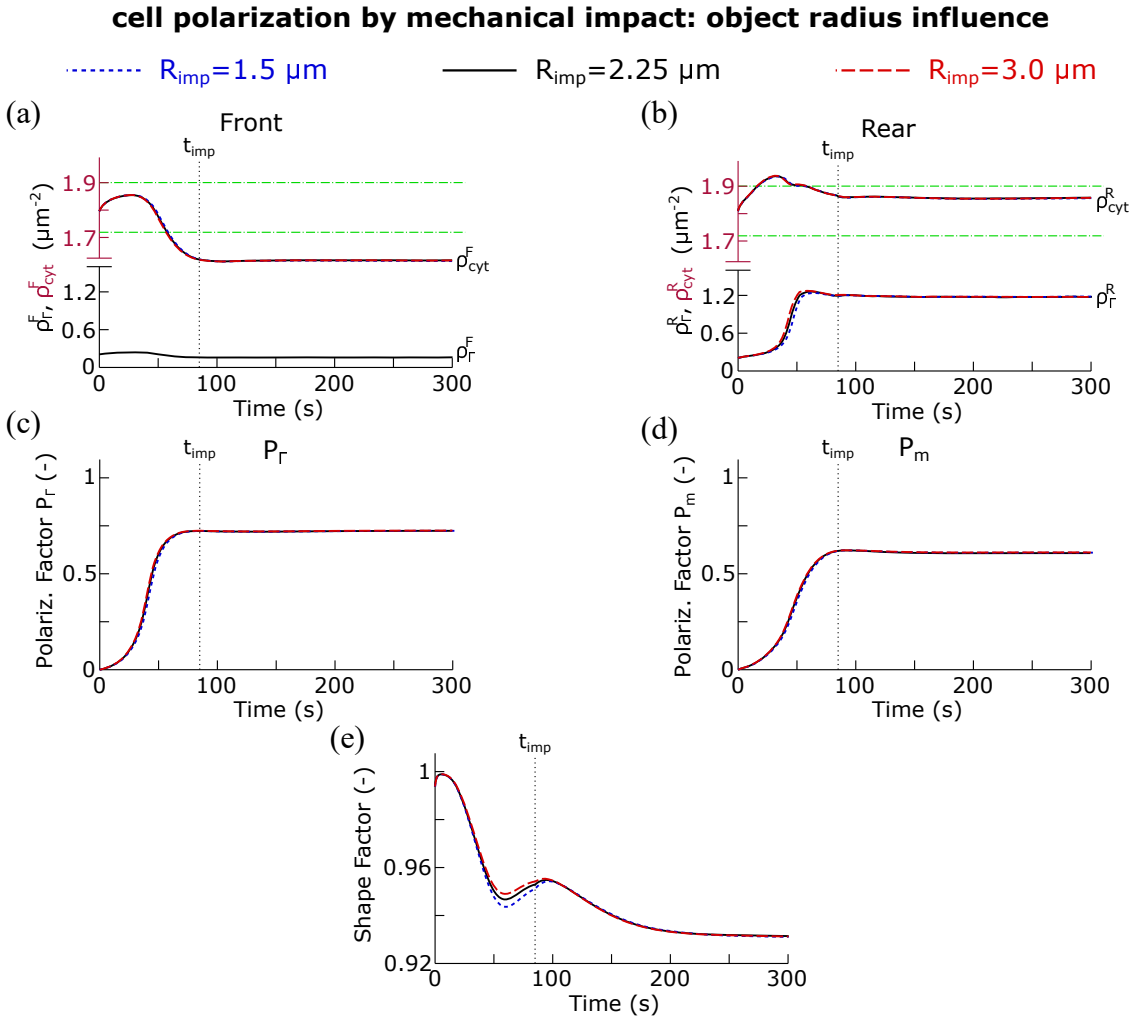

Fig. S7 Influence of the pushing object radius (R_{imp}) on cell polarization by mechanical impact. Time evolution of *(a)* ρ^F_{cyt} and ρ^F_Γ; *(b)* ρ^R_{cyt} and ρ^R_Γ; *(c)* P_Γ; *(d)* P_m; and *(e)* cellular shape factor for three simulations with $R_{\mathrm{imp}} = 1.5$ (blue dotted line), 2.25 (black solid line), and 3.0μm (red dashed line). The vertical dotted line in the graphs indicates the time t_{imp}, time at which the pushing force vanishes. The influence of the radius R_{imp} is very small.

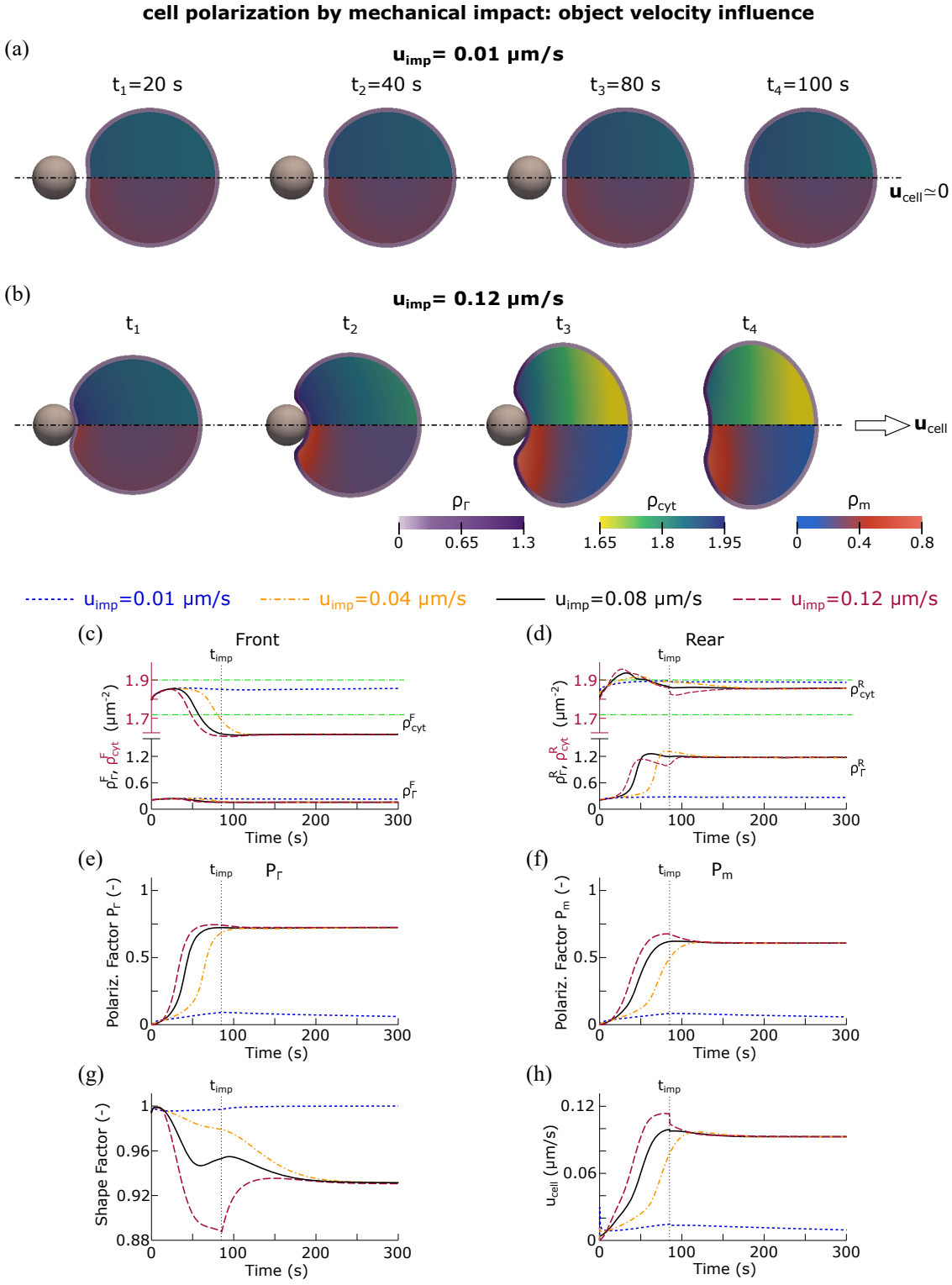

Fig. S8 Influence of the pushing object velocity (u_{imp}) on cell polarization by mechanical impact. ρ_Γ, ρ_{cyt}, and ρ_m distributions at times $t_1 = 20$, $t_2 = 40$, $t_3 = 80$, and $t_4 = 100\,\mathrm{s}$ for two simulations with *(a)* $u_{\mathrm{imp}} = 0.01$ and *(b)* $u_{\mathrm{imp}} = 0.12\,\mu\mathrm{m\,s^{-1}}$. Time evolution of *(c)* ρ^F_{cyt} and ρ^F_Γ; *(d)* ρ^R_{cyt} and ρ^R_Γ; *(e)* P_Γ; *(f)* P_m; *(g)* SF; and *(h)* u_{cell} for four simulations with $u_{\mathrm{imp}} = 0.01$ (blue dotted line), 0.04 (yellow dash-dotted line), 0.08 (black solid line), and $0.12\,\mu\mathrm{m\,s^{-1}}$ (red dashed line). The vertical dotted line in the graphs indicates the time t_{imp}. The sharp transition of the plots at t_{imp} is due to the sudden removal of the pushing force. Small u_{imp} does not produce a steady polarized state. As u_{imp} increases, the cell polarizes faster.

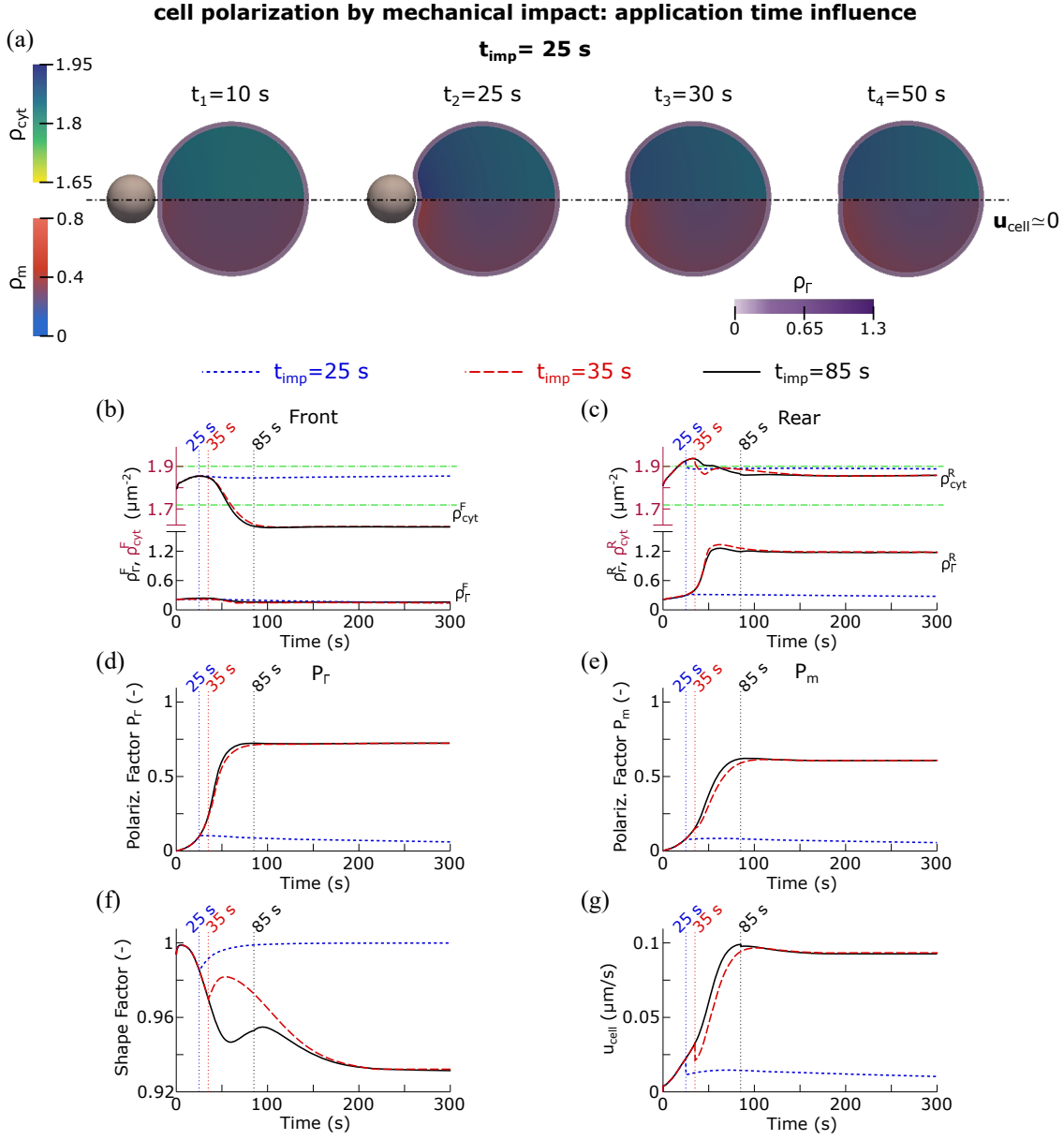

Fig. S9 Influence of the application time (t_{imp}) of the pushing object on cell polarization by mechanical impact. The layout of the figure is analogous to Fig. S8. *(a)* ρ_Γ, ρ_{cyt}, and ρ_m distributions at four different times. Time evolution of *(b)* ρ^F_{cyt} and ρ^F_Γ; *(c)* ρ^R_{cyt} and ρ^R_Γ; *(d)* P_Γ; *(e)* P_m; *(f)* SF; and *(g)* u_{cell} for three simulations with $t_{\mathrm{imp}} = 25$ (blue dotted line), 35 (red dashed line), and 85 s (black solid line). The vertical dotted lines in the graphs indicate the corresponding t_{imp}: 25 (blue), 35 (red), and 85 s (black). Short t_{imp} can not induce a steady polarized state. The results show that there is a threshold of t_{imp} to achieve cell polarization. Once the cell reaches that threshold, the influence of t_{imp} is small (compare P_Γ and P_m for $t_{\mathrm{imp}} = 35$ and 85 s).

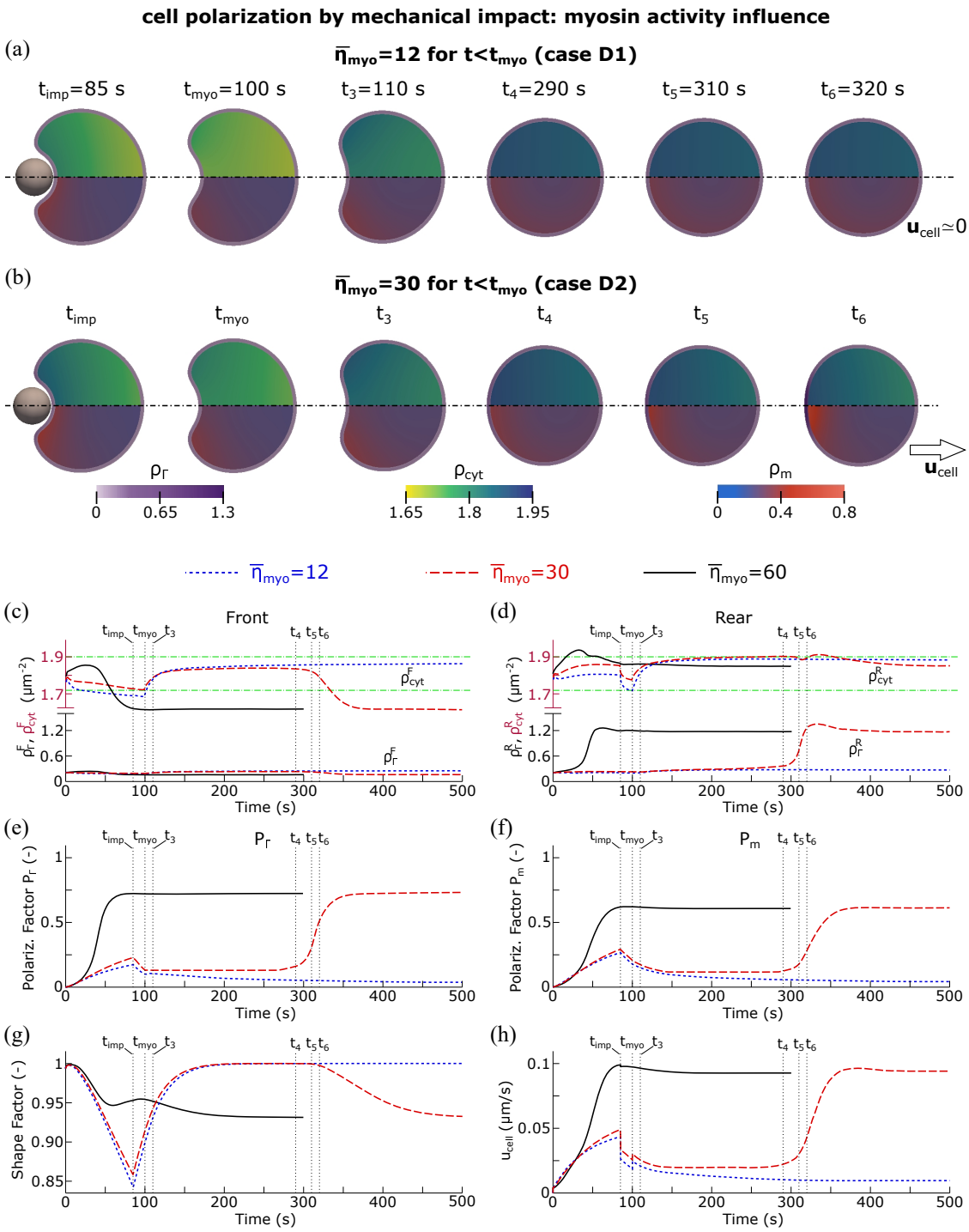

Fig. S10 Influence of myosin inhibition on cell polarization by mechanical impact. Myosin activity is downregulated in the entire cell for $t < t_{\mathrm{myo}} = 100\,\mathrm{s}$. The pushing force vanishes at $t_{\mathrm{imp}} = 85\,\mathrm{s}$. The layout of the figure is analogous to Fig. S8. ρ_Γ, ρ_{cyt}, and ρ_m distributions at times $t_{\mathrm{imp}} = 85$, $t_{\mathrm{myo}} = 100$, $t_3 = 110$, $t_4 = 290$, $t_5 = 310$, and $t_6 = 320\,\mathrm{s}$ for two simulations with *(a)* $\overline{\eta}_{\mathrm{myo}} = 12\,\mathrm{pN}\mu\mathrm{m}$ (case D1) and *(b)* $\overline{\eta}_{\mathrm{myo}} = 30\,\mathrm{pN}\mu\mathrm{m}$ (case D2). Time evolution of *(c)* ρ^F_{cyt} and ρ^F_Γ; *(d)* ρ^R_{cyt} and ρ^R_Γ; *(e)* P_Γ; *(f)* P_m; *(g)* SF; and *(h)* u_{cell} for three simulations with $\overline{\eta}_{\mathrm{myo}} = 12$ (blue dotted line), 30 (red dashed line), and $60\,\mathrm{pN}\mu\mathrm{m}$ (black solid line). We stop the simulations with $\overline{\eta}_{\mathrm{myo}} = 12$ and $30\,\mathrm{pN}\mu\mathrm{m}$ at $t = 600\,\mathrm{s}$ rather than $300\,\mathrm{s}$ so that the simulations can achieve a steady state. The vertical dotted lines in the graphs indicate the times t_{imp}, t_{myo}, t_3, t_4, t_5, and t_6. Strong levels of myosin inhibition impede the polarization of the cell.

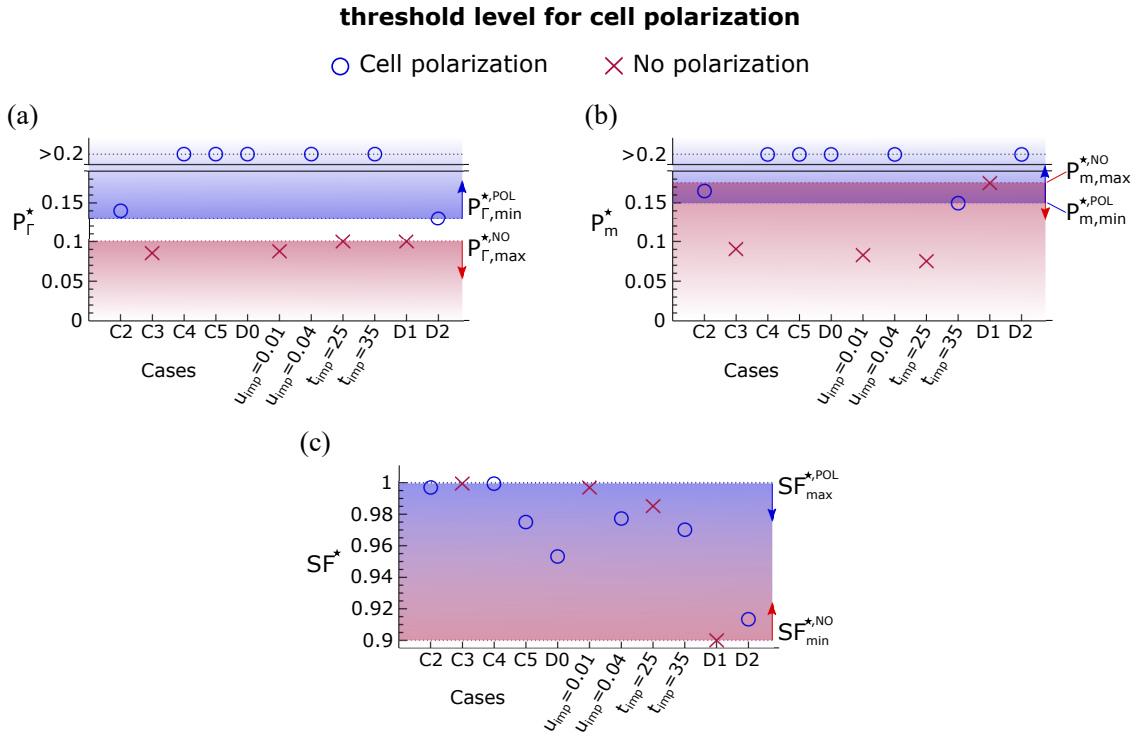

Fig. S11 Estimation of the threshold level for cell polarization induced by external stimuli. We computed P_Γ, P_m, and SF at the time the external stimuli vanish, denoted as $P_\Gamma^\star$, $P_m^\star$, and $SF^\star$, respectively, for cases C2, C3, C4, C5, D0, D1, D2, and the cases of cell polarization by mechanical impact with $u_{\text{imp}} = 0.01\,\mu\text{m}\,\text{s}^{-1}$ and $u_{\text{imp}} = 0.04\,\mu\text{m}\,\text{s}^{-1}$ (see Fig. S8), and $t_{\text{imp}} = 25\,\text{s}$ and $t_{\text{imp}} = 35\,\text{s}$ (see Fig. S9). *(a)* $P_\Gamma^\star$; *(b)* $P_m^\star$; and *(c)* $SF^\star$ for the cases analyzed. Blue circles represent cells that achieve a steady polarized state. Red crosses represent cells that do not polarize. We define the region of no polarization (red shaded region) as the points $P_\Gamma^\star$, $P_m^\star$, and $SF^\star$ such that $P_\Gamma^\star < P_{\Gamma,\text{max}}^{\star,\text{NO}}$, $P_m^\star < P_{m,\text{max}}^{\star,\text{NO}}$, and $SF^\star > SF_{\text{min}}^{\star,\text{NO}}$, respectively, where $P_{\Gamma,\text{max}}^{\star,\text{NO}}$ is the maximum $P_\Gamma^\star$, $P_{m,\text{max}}^{\star,\text{NO}}$ the maximum $P_m^\star$, and $SF_{\text{min}}^{\star,\text{NO}}$ the minimum $SF^\star$ of non-polarized cells (red crosses). Likewise, we define the region of cell polarization (blue shaded region) as the points $P_\Gamma^\star$, $P_m^\star$, and $SF^\star$ such that $P_\Gamma^\star > P_{\Gamma,\text{min}}^{\star,\text{POL}}$, $P_m^\star > P_{m,\text{min}}^{\star,\text{POL}}$, and $SF^\star < SF_{\text{max}}^{\star,\text{POL}}$, respectively, where $P_{\Gamma,\text{min}}^{\star,\text{POL}}$ is the minimum $P_\Gamma^\star$, $P_{m,\text{min}}^{\star,\text{POL}}$ the minimum $P_m^\star$, and $SF_{\text{max}}^{\star,\text{POL}}$ the maximum $SF^\star$ of polarized cells (blue circles). If there is a threshold level for cell polarization, the blue and red shaded regions can not overlap. The hypothesis of a threshold level for cell polarization only holds for P_Γ. The threshold is between $P_{\Gamma,\text{max}}^{\star,\text{NO}} = 0.1$ and $P_{\Gamma,\text{min}}^{\star,\text{POL}} = 0.13$.