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**S.1 A general description of the polarization model for an individual cell.**

The model considers the dynamics of two actin networks competing for molecular resources and coupled to the dynamics of active, membrane-bound Rac and Rho molecules. In the model, the dynamics is localized to the periphery of the the disc-shaped cell adhering to a substrate, and so the molecular densities are localized to the circle of circumferential length .

**Actin dynamics.**

The cytoskeletal model is a competition of two distinct actin networks with the following dynamics:

1. *Autocatalytic growth:* The net growth rate of each network is proportional to local network density. This assumption is based on the processes of polymerization of existent actin filaments and of nucleation of nascent filaments by proteins binding to the existent filaments, so that the net growth becomes proportional to the existent density.
2. *Limited growth*: At high density, growth is limited due to lack of availability of molecular resources. In the case of the bundled actin network, growth could be limited due to depletion of the myosin-II motors or actin monomers, while the branched actin network growth could be limited by availability of Arp2/3 branching complexes or globular actin monomers.
3. *Competition for molecular resources*: Both networks compete for a limited cytoplasmic pool of molecular resources, such as G-actin monomers, Arp2/3 complexes, formins or myosin.
4. *Diffusive-driven redistribution of the networks along the cell boundary*: We assume, following [Lomakin2015], an effective diffusive spread of actin densities along the cell edge due to lateral shifts of the actin density due to filament growth and/or to physical sliding of filaments along the cell edge pulled by myosin motors.

Mathematically, based on these assumed dynamics one arrives at the following set of non-dimensionalized PDEs [Lomakin2015]:

Here denotes the branched actin network density and represents the bundled actin network density along the cell boundary parameterized by the arc length . Densities of both actin networks are defined on the periodic cell boundary. is the non-dimensional competition parameter, and is the non-dimensional diffusion coefficient. Note that this effective diffusion coefficient is the result of an effective random walk of the growing ends of branched filaments along the cell edge. There filaments are growing skewed to the left and right, and thus glide along the cell edge for about a second before being capped, and then daughter filaments glide in opposite directions. For bundled filaments, the diffusion originates from the myosin-powered shuffling of the filaments along the cell edge. Respective diffusion coefficients have the same order of magnitude analyzed in [Lomakin2015]. Note also that we chose to model the cytoskeleton in a continuous, deterministic way, because the estimate for the number of actin on the cell edge, [Abraham1999] is much higher than the estimate for the number of signaling molecules on the membrane: in the whole cell, of which is on the membrane [Walther2012].

Although Eq. S1 represent conservation laws for the two actin networks, we can also use the balance of forces to justify the mechanical nature of expressions for some parameters in this model and identify the connection to physical/mechanical forces including myosin contractile force, membrane tension, and effective friction from adhesion of the actin networks to the substrate. Specifically, small, and dynamic nascent adhesions based on integrin molecules spanning the cell membrane interconnect the branched actin and the substrate. More mature focal adhesions, also integrin based but including many adaptors, force-sensing and signaling molecules, connect actomyosin bundles with themselves and the substrate. Besides the kinetic effect contributing to the term -- the competition of the branched and bundled actin networks for the same G-actin monomer pool -- there are also underlying mechanical processes. In the update equation for the branched actin network (Eq. S1a), the competition term, , describes the rate at which branched filaments are incorporated into anti-parallel contractile actin bundles in the presence of myosin motors. The rate is proportional to the actomyosin density. The competition term in the update equation for bundled acto-myosin network (Eq. S1b) has a similar mechanical underpinning. The expression is the rate of removal of the bundled actin by the flow generated by branched actin filaments growing against the membrane at the cell edge and centripetally pushing the bundles away from the edge. The rate is proportional to the branched actin density because of the force balance between the membrane tension and strength of adhesions of the bundled actin to the substrate. Assuming a viscous behavior of adhesions, the centripetal flow rate is where is the adhesion strength while is the membrane tension. The membrane tension which is likely to be proportional to the density of branched filaments pushing on the membrane from within, hence the centripetal flow is proportional to the density of branched actin network [Mogilner1996].

**Signaling molecule dynamics.**

We focus on the mutually exclusive interactions between Rac and Rho on the plasma membrane. Following the rationale of the stochastic model proposed by Altschuler et al. [Altschuler], we assume five different kinds of molecular events:

1. *Spontaneous association to the membrane*: GTP-bound Rho GTPase proteins undergo a conformational change and transition to an active membrane-bound state. We model this by an association of a respective molecule from the cytosol to a random location on the membrane at a rate of .
2. *Spontaneous disassociation from the membrane*: GAP proteins regulate the transition of active, membrane-bound Rho GTPase into an inactive, cytosolic state. This event is modeled through the removal of an active molecule from the membrane at a rate of
3. *Enhanced membrane association through activators*: Local positive feedback loops are thought to play a role in sustaining nascent Rac/Rho sites on the plasma membrane [Ngu,Nei,Ino,Wei]. To model these feedback loops we assume that a membrane-bound (active) molecule of either type (Rac or Rho) can indirectly activate and recruit a molecule of the same type to its vicinity. The rate at which one molecule recruits from the cytosol is proportional to the fraction of molecules which are still in the cytosol with a proportionality constant of .
4. *Diffusion on the membrane*: Each molecule on the membrane undergoes a Brownian motion with diffusion coefficient
5. *Steric interaction*: In the association, recruitment, and diffusive processes, Rac and Rho proteins cannot occupy the same location in space at a given time. This assumption is based on the reported mutual antagonistic interactions between Rho GTPases [Byr, Gui, Bur, Xu, van, Wan].

We first outline the algorithm implementation for the Rac/Rho dynamics when the kinetic rates are constant in space. The system is initialized with 10% of the total number of signaling molecules of each type (Rac/Rho), . These initial molecules are randomly placed along the cell membrane ensuring that particles of different type do not spatially overlap. The number of Rac (or Rho) particles on the cell membrane, evolves by a Poisson process. Because the signaling dynamics will eventually be coupled to spatially varying actin concentrations, we consider individual rather than aggregate transition rates. For each membrane- bound particle , the time and location of the next biochemical reaction event is computed discretely. In particular, the time to the next reaction for membrane- bound particle is exponentially distributed with rate:

The next reaction time is computed for all membrane-bound particles, , and the minimum time is chosen across all active particles of a given type. Then, for the particle with the lowest reaction time, either a disassociation event with probability or a spontaneous association event with probability or an enhanced association event with has occurred. If a disassociation event has taken place, this particles is removed from the membrane and added to the cytoplasmic pool of well-mixed, homogeneous inactive particles. If an enhanced recruitment association event has occurred, an inactive particle is moved to the membrane and its location coincides with the already membrane-bound particle. Lastly, for a spontaneous association event, an inactive particle is moved to the membrane to a location chosen randomly halfway between its nearest neighboring particles of the same type. This process is repeated independently for both Rac and Rho species. The probability for the number of particles of each type can be expressed via a master equation as given in Altschuler et al. [Alt]. However, we note that to our knowledge no such master equation can be easily expressed in the case of spatially varying kinetic rates. In the presence of the mechanochemical coupling, the kinetic rates depend on position on the cell edge, and the algorithm is modified as discussed below.

**Mechanochemical coupling.**

For the mutual coupling between actin cytoskeleton and polarity molecules, we assume that there is a local feedback loop with a linear dependence on relative concentrations. The chemical rates in the signaling kinetics are no longer constant but rather dependent on the local concentration of each respective actin network which evolves in both space and time. We assume that Rac and the branched actin network engage in a positive feedback loop and similarly so do Rho and the bundled actomyosin mesh by modifying the kinetic rates of Rac and Rho as follows:

where represents the strength of the coupling from the polarity molecules to the cytoskeleton.

In principle, other choices for actin dependence on the signaling kinetic rates could have been introduced -- for example, if only one of these three parameters () is sensitive to feedback from actin, while the other two are constant (or only two are actin-dependent, or all three). We found that when the actin dependence appears only in the enhanced recruitment rate, , the model shows a high polarization probability (90%), instead of 100% polarization probability. However, when actin dependence is removed from the enhanced recruitment association rate, while the other two rates do depend on actin, the polarization probability falls below 10%. This result indicates that other spatial dependencies of kinetic rates could have been chosen, but the results presented here are for the particular choice in Eqs. S3-S6.

PARAM TABLE

**Numerical simulations.**

The theoretical approach provided above could describe the actin networks concentration and polarity molecules on a one-dimensional curve or a two-dimensional surface of the plasma membrane. The numerical simulations carried out here were on one-dimensional circles for ease of visualization, but we believe the results here could be reproduced in higher dimensions on arbitrary geometries. To simulate the dynamics of cell polarization, the computational domain representing concentrations in the plasma membrane and a thin volume of cytoplasm adjacent to the membrane is discretized using 101 points with an averaged spatial discretization of . The temporal discretization is and simulations are run to 30-100 seconds. The codes are written and solved in Matlab. Model parameters along with justifications for the choice of values are provided in supplementary material, Table S1. We perform simulations using the baseline parameter values listed in Table S1, unless otherwise indicated. The computational code is freely available online on a Github public repository: https://github.com/CoposLab/Co-polarity.

The actin dynamics PDEs in Eq. S1 are solved on a circular domain using Crank-Nicolson finite difference numerical method with periodic boundary conditions. The actin networks are randomly distributed initially with equal relative concentrations between branched and bundled networks.

A modified Gillespie algorithm is used for the next reaction time for the polarity molecules. The time between Markov jumps is exponentially distributed with individual rate as provided in Eq.S2. In between the jumps, the molecules with locations and , where is the index of the specific molecule, undergo Brownian motion on the membrane with diffusion coefficient : . Since we enforce segregation of Rac and Rho, collisions between a Rac molecule and a Rho molecule in the diffusive process may occur. We resolve collision events by not allowing either molecule to move into the space (interval of width around a given molecule) that would result in overlap (collisions between Rac and Rac or Rho and Rho molecules are tolerated). Other more sophisticated collision resolution methods could have been employed, but for simplicity we chose this minimal dynamic. We have assessed what would happen in the absence of any such steric interaction, by running 20 simulations without any collision detection (with default values for all other parameters) and found a polarization probability of 95% (when such probability is 100% in the presence of steric interaction). In the instances of polarity establishment, the cell polarizes by actin dynamics but with less well-defined peaks in Rac and Rho concentrations as illustrated in Fig. S3. Thus, it seems that the assumed steric repulsion is helpful for the polarization (by assisting spatial segregation of Rac and Rho), but not necessary to the overall results of the model.

**The doublet model.**

The model is extended to a pair of cells by implementing two copies of the single cell model simultaneously, where each cell has its own mechanical and biochemical networks. A contact region is defined between the two cells as 25% of the cell membrane in each cell. We denote the cell on the left as ``Cell 1" and the cell on the right as ``Cell 2." The contact region is centered at 270° counterclockwise from the top of the cell in Cell 1 and centered at 90° in Cell 2. All pathways of communication between the two cells are implemented only in this contact region. The polarity axis of each cell is defined as an angle counterclockwise from the top of the cell. When a cell polarizes, we threshold the region of the cell membrane where the concentration of branched actin is greater than . The median point in this region gives the polarity axis.

S.2 Model results for speculated pathways for cell-cell coupling

Description of hypotheses and interpretations

Description of mutual Rac-Rho antagonism

Description of implementation of CIL, COA, CIL&COA

S.2 Model results for concentration-dependent

S.3 Model results for signal switch