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# Supplemental Information

## Spherical Caps in Cell Polarization

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### Supporting Material: Spherical caps in cell polarization

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#### Axisymmetric Steady States

In this section, we derive the steady state solutions in the form of axisymmetric caps for a given set of model parameters  $(\alpha, \beta, \gamma, \delta)$ . Equation (8) in the main text is an ODE that defines  $u = \bar{u}(\eta)$  on the surface of the sphere at steady state:

$$
0 = \delta^2 \frac{d}{d\eta} \left[ (1 - \eta^2) \frac{d\bar{u}}{d\eta} \right] + \left( 1 - \alpha \int_{-1}^1 \bar{u} \, d\eta \right) (\beta + H(\bar{u} - \gamma)) - \bar{u}.
$$
 (S1)

By inspection, this ODE yields two stable uniform solutions  $u = u_{\pm}$  lying below and above the threshold  $u = \gamma$ , respectively:

<span id="page-1-3"></span><span id="page-1-2"></span>
$$
u_{-} = \frac{\beta}{1 + 2\alpha\beta}
$$
 and  $u_{+} = \frac{1 + \beta}{1 + 2\alpha(1 + \beta)}$ . (S2)

In addition to these uniform steady states, nonuniform solutions may also exist, corresponding to polarized patterns on the sphere. Without loss of generality, the isotropy of the sphere allows us to define our  $\eta$  axis such that the cap is centered at  $\eta = -1$  and  $\bar{u}(\eta)$  is monotonically decreasing. For these cap-like profiles to exist, there must exist some regions where  $\bar{u}(\eta) > \gamma$  and  $\bar{u}(\eta) < \gamma$ , respectively. Continuity and monotonicity of the profile therefore imply the existence of some  $\eta = \eta_c \in (-1,1)$  such that  $\bar{u}(\eta_c) = \gamma$ . The ODE may then be split into two distinct regions, corresponding to the presence or absence of autocatalytic recruitment:

$$
0 = \delta^2 \frac{d}{d\eta} \left[ (1 - \eta^2) \frac{d\bar{u}}{d\eta} \right] + k\beta - \bar{u}, \qquad \eta > \eta_c,
$$
 (S3)

$$
0 = \delta^2 \frac{d}{d\eta} \left[ (1 - \eta^2) \frac{d\bar{u}}{d\eta} \right] + k \left( \beta + 1 \right) - \bar{u}, \qquad \eta < \eta_c,\tag{S4}
$$

where we introduced a constant

<span id="page-1-4"></span><span id="page-1-1"></span><span id="page-1-0"></span>
$$
k := 1 - \alpha \int_{-1}^{1} \bar{u} \, d\eta,
$$
 (S5)

that depends on the solution  $\bar{u}(\eta)$ .

We now solve the nonhomogeneous Equations [\(S3\)](#page-1-0)-[\(S4\)](#page-1-1). When  $\eta > \eta_c$ :

<span id="page-2-0"></span>
$$
\frac{d}{d\eta} \left[ (1 - \eta^2) \frac{d\bar{u}}{d\eta} \right] - \frac{\bar{u}}{\delta^2} = -\frac{k\beta}{\delta^2},\tag{S6}
$$

whose particular solution is  $u_p = k\beta$ . The corresponding homogeneous ODE is of the form:

$$
\frac{d}{d\eta} \left[ (1 - \eta^2) \frac{d\bar{u}}{d\eta} \right] + \mu(\mu + 1)\bar{u} = 0, \qquad \mu := -\frac{1}{2} + \frac{1}{2} \sqrt{1 - \frac{4}{\delta^2}}.
$$
 (S7)

One solution of this equation is given by  $P_{\mu}(\eta)$ , the Legendre function of the first kind, defined as

$$
P_{\mu}(\eta) = {}_{2}F_{1}\left(-\mu, \mu+1; 1; \frac{1-\eta}{2}\right), \tag{S8}
$$

where  ${}_2F_1(a, b; c; z)$  is the hypergeometric function [\[1\]](#page-18-0). Explicitly, using the definition of  $\mu$ (irrespectively of the choice of the analytic branch for  $\delta < 2$ ) and the power series representation of the hypergeometric function we have

<span id="page-2-1"></span>
$$
P_{\mu}(\eta) = 1 + \sum_{n=1}^{\infty} \frac{(1-\eta)^n}{2^n (n!)^2} \prod_{l=0}^{n-1} (l-\mu)(l+1+\mu)
$$
  
=  $1 + \sum_{n=1}^{\infty} \frac{(1-\eta)^n}{2^n (n!)^2} \prod_{l=0}^{n-1} \left(\frac{1}{\delta^2} + l + l^2\right),$  (S9)

where the series above converges absolutely for all  $\eta \in (-1,1)$ . Furthermore, by direct inspection of this formula we have  $P_{\mu}(1) = 1$ ,  $P_{\mu}(-1) = \infty$ , and  $P_{\mu}(\eta)$  is real-valued and strictly decreasing for all  $\eta \in (-1,1)$ . Therefore, in view of the reflection symmetry the second linearly independent solution of the above equation may be chosen to be  $P_{\mu}(-\eta)$ , and the general solution of Equation [\(S3\)](#page-1-0) may be written as

$$
\bar{u}(\eta > \eta_c) = c_1 P_\mu(\eta) + c_2 P_\mu(-\eta) + k\beta,
$$
\n(S10)

for some constants  $c_{1,2}$ . Boundedness of the solution for  $\eta > \eta_c$  implies that  $c_2 = 0$  and monotonicity of the profile requires that  $c_1 > 0$ . In addition, for some  $\eta_c \in (-1,1)$  we should have  $\bar{u}(\eta_c) = \gamma$ . This yields for  $\gamma > \beta k$ :

$$
\bar{u}(\eta > \eta_c) = \frac{\gamma - \beta k}{P_\mu(\eta_c)} P_\mu(\eta) + k\beta.
$$
\n(S11)

Equation [\(S4\)](#page-1-1) may be solved in the same manner when  $\eta < \eta_c$ :

$$
\frac{d}{d\eta} \left[ (1 - \eta^2) \frac{d\bar{u}}{d\eta} \right] - \frac{\bar{u}}{\delta^2} = -\frac{k(\beta + 1)}{\delta^2}.
$$
\n(S12)

A particular solution is  $u_p = k(\beta + 1)$ , and the homogeneous equation is as before. Thus, the general solution is now:

$$
\bar{u}(\eta < \eta_c) = c_3 P_\mu(-\eta) + c_4 P_\mu(\eta) + k(\beta + 1),\tag{S13}
$$

for some constants  $c_{3,4}$ . Boundedness and monotonicity imply  $c_4 = 0$  and  $c_3 < 0$ , and the condition that  $\bar{u}(\eta_c) = \gamma$  yields:

$$
\bar{u}(\eta < \eta_c) = \frac{\gamma - (1 + \beta)k}{P_\mu(-\eta_c)} P_\mu(-\eta) + k(1 + \beta). \tag{S14}
$$

Thus, we arrive at the nonuniform steady state solution in Equations (9)-(10) from the main text:

<span id="page-3-0"></span>
$$
\bar{u}(\eta > \eta_c) = (\gamma - \beta k) \frac{P_\mu(\eta)}{P_\mu(\eta_c)} + \beta k,
$$
\n(S15)

$$
\bar{u}(\eta < \eta_c) = (\gamma - (1 + \beta)k) \frac{P_\mu(-\eta)}{P_\mu(-\eta_c)} + (1 + \beta)k. \tag{S16}
$$

Smoothness at of the solution at  $\eta = \eta_c$  requires matching first derivatives. Differentiating Equations [\(S15\)](#page-3-0)-[\(S16\)](#page-3-1) with respect to  $\eta$  and setting the two sides equal at  $\eta = \eta_c$  yields an explicit equation for  $k$  in terms of model parameters that matches the relationship given in the main text:

<span id="page-3-8"></span><span id="page-3-2"></span><span id="page-3-1"></span>
$$
k = \frac{\gamma \left( 1 + \frac{P_{\mu}^{\prime}(\eta_c)}{P_{\mu}^{\prime}(-\eta_c)} \frac{P_{\mu}(-\eta_c)}{P_{\mu}(\eta_c)} \right)}{1 + \beta \left( 1 + \frac{P_{\mu}^{\prime}(\eta_c)}{P_{\mu}^{\prime}(-\eta_c)} \frac{P_{\mu}(-\eta_c)}{P_{\mu}(\eta_c)} \right)}.
$$
(S17)

Multiplying this expression through Equation [\(S16\)](#page-3-1) allows  $\bar{u}(\eta < \eta_c)$  to be written in a more convenient form that will allow for an expression for  $\gamma$  in terms of model parameters:

$$
\bar{u}(\eta < \eta_c) = (\beta k - \gamma) \frac{P'_{\mu}(\eta_c)}{P'_{\mu}(-\eta_c)} \frac{P_{\mu}(-\eta)}{P_{\mu}(\eta_c)} + (1 + \beta)k. \tag{S18}
$$

Using Equation [\(S18\)](#page-3-2) and the original definition of  $k$  defined for Equations [\(S3\)](#page-1-0)-[\(S4\)](#page-1-1) yields an integral equation that relates all model parameters:

$$
\frac{\alpha\left(\gamma-\beta k\right)}{P_{\mu}(\eta_c)}\left[-\frac{P'_{\mu}(\eta_c)}{P'_{\mu}(-\eta_c)}\int_{-1}^{\eta_c}P_{\mu}(-\eta)\,\mathrm{d}\eta+\int_{\eta_c}^1P_{\mu}(\eta)\,\mathrm{d}\eta\right]+k(1+\alpha(1+\eta_c)+2\alpha\beta)=1.\tag{S19}
$$

Equations [\(S20\)](#page-3-3)-[\(S23\)](#page-3-4) highlight known properties of Legendre functions that allow for Equation [\(S19\)](#page-3-5) to be simplified further:

$$
\int_{x}^{1} P_{\mu}(\eta) d\eta = \frac{P_{\mu-1}(x) - P_{\mu+1}(x)}{2\mu + 1},
$$
\n(S20)

<span id="page-3-7"></span><span id="page-3-6"></span><span id="page-3-5"></span><span id="page-3-4"></span><span id="page-3-3"></span>
$$
P'_{\mu}(x) = \frac{\mu + 1}{1 - x^2} \left( x P_{\mu}(x) - P_{\mu+1}(x) \right),\tag{S21}
$$

$$
P'_{\mu}(-x) = -\frac{\mu+1}{1-x^2} \left( x P_{\mu}(-x) + P_{\mu+1}(-x) \right), \tag{S22}
$$

$$
(2\mu + 1)xP_{\mu}(x) = \mu P_{\mu-1}(x) + (\mu + 1)P_{\mu+1}(x).
$$
 (S23)

The integral expressions in Equation [\(S19\)](#page-3-5) may be rearranged as

$$
-\frac{P'_{\mu}(\eta_c)}{P'_{\mu}(-\eta_c)} \int_{-1}^{\eta_c} P_{\mu}(-\eta) d\eta + \int_{\eta_c}^1 P_{\mu}(\eta) d\eta = -\frac{P'_{\mu}(\eta_c)}{P'_{\mu}(-\eta_c)} \int_{-\eta_c}^1 P_{\mu}(y) dy + \int_{\eta_c}^1 P_{\mu}(\eta) d\eta.
$$
\n(S24)

Dividing all the terms in Equation [\(S23\)](#page-3-4) by  $\mu$  allows one to write  $P_{\mu-1}(x)$  in terms of  $P_{\mu}(x)$ . This expression can be plugged into the definition of the integral in Equation [\(S20\)](#page-3-3). The definitions of the derivatives given in Equations [\(S21\)](#page-3-6)-[\(S22\)](#page-3-7) yield the relationship given in Equation [\(S25\)](#page-4-0):

<span id="page-4-0"></span>
$$
-\frac{P'_{\mu}(\eta_c)}{P'_{\mu}(-\eta_c)} \int_{-\eta_c}^{1} P_{\mu}(y) \, dy + \int_{\eta_c}^{1} P_{\mu}(\eta) \, d\eta = 0.
$$
 (S25)

Substituting this result into Equation  $(S19)$  and using the expression for k given by Equa-tion [\(S17\)](#page-3-8) allows for  $\gamma$  to be expressed in terms of the model parameters, the key result of this analysis given as Equation (11) in the main text:

<span id="page-4-1"></span>
$$
\gamma = \frac{1 + \beta \left( 1 + \frac{P_{\mu}^{\prime}(\eta_c)}{P_{\mu}^{\prime}(-\eta_c)} \frac{P_{\mu}(-\eta_c)}{P_{\mu}(\eta_c)} \right)}{\left( 1 + \frac{P_{\mu}^{\prime}(\eta_c)}{P_{\mu}^{\prime}(-\eta_c)} \frac{P_{\mu}(-\eta_c)}{P_{\mu}(\eta_c)} \right) \left( 1 + \alpha (1 + \eta_c) + 2\alpha \beta \right)}.
$$
\n(S26)

Existence and multiplicity of solutions of Equation [\(S1\)](#page-1-2) is determined by the roots of the algebraic equation above and can be analyzed graphically for any specific set of the parameters  $(\alpha, \beta, \gamma, \delta)$ . As discussed in the main text, depending on the values of the parameters we generically find 1 or 3 distinct roots for Equation [\(S26\)](#page-4-1), with the latter case observed for smaller values of  $\delta$ . To see whether this situation persists, we carried out an asymptotic analysis of solutions of Equation [\(S26\)](#page-4-1) for an important parameter regime of  $\delta \ll 1$ , in which the spherical cap profiles are characterized by sharp concentration gradients. In this case one can use WKB asymptotics of the Legendre functions (as obtained from Equation [\(S7\)](#page-2-0)) to see that to the leading order

$$
P_{\mu}(\eta)/P_{\mu}(0) \simeq (1 - \eta^2)^{-1/4} e^{-\delta^{-1} \arcsin \eta}, \qquad \eta \in (-1, 1), \tag{S27}
$$

and, therefore, we have  $P'_{\mu}(\eta)/P_{\mu}(\eta) \simeq -1/\left(\delta\sqrt{1-\eta^2}\right)$  for all  $1-\eta^2 \gg \delta^2$  and  $\delta \ll 1$ . Substituting this expression into Equation [\(S26\)](#page-4-1) yields for all  $1-\eta_c^2 \gg \delta^2$  and all  $\delta$  sufficiently small:

<span id="page-4-2"></span>
$$
\gamma(\eta_c) \simeq \frac{2\beta + 1}{2(1 + \alpha(2\beta + 1 + \eta_c))}.\tag{S28}
$$

A comparison between Equation [\(S26\)](#page-4-1) and the scaling given by Equation [\(S28\)](#page-4-2) in Figure [S1](#page-5-0) shows reasonable agreement when  $\eta_c$  is far away from the ends of the domain. In particular,



<span id="page-5-0"></span>Figure S1: For  $\alpha = 1, \beta = 0.1$ , the curves defined by Equations [S26](#page-4-1) and [S28](#page-4-2) Here, it can be seen that this scaling is accurate for sufficiently small  $\delta$  in the regime where  $\gamma(\eta_c)$  in Equation [S26](#page-4-1) has a negative slope.

 $\gamma(\eta_c)$  is a monotone decreasing function with  $\gamma \in \left(\frac{2\beta+1}{2(1+2\alpha(\beta+1))}, \frac{2\beta+1}{2(1+2\alpha)}\right)$  $\frac{2\beta+1}{2(1+2\alpha\beta)}$ . We refer to this branch of solutions as *large spherical caps*, in which the profile  $\bar{u}(\eta)$  approaches a piecewiseconstant function taking both values from Equation [\(S2\)](#page-1-3). On the other hand, one can see from Equation [\(S9\)](#page-2-1) that to the leading order in  $\delta \ll 1$  we have

$$
P_{\mu}(\eta) \simeq \sum_{n=0}^{\infty} \frac{(1-\eta)^n}{2^n \delta^{2n} (n!)^2} = I_0\left(\sqrt{2\delta^{-2}(1-\eta)}\right), \qquad 1-\eta = O(\delta^2), \tag{S29}
$$

where  $I_0(z)$  is the modified Bessel function of the first kind [\[1\]](#page-18-0). This formula can also be obtained by rewriting Equation [\(S7\)](#page-2-0), using the variable  $z = \arccos \eta$  and keeping only the leading order terms. Similarly, to the leading order in  $\delta \ll 1$  we have

$$
P_{\mu}(\eta) \sim K_0 \left(\sqrt{2\delta^{-2}(1+\eta)}\right), \qquad 1+\eta = O(\delta^2), \tag{S30}
$$

where  $K_0(z)$  is the modified Bessel function of the second kind [\[1\]](#page-18-0). With this information at hand, we have for  $\delta \ll 1$ :

$$
\frac{P'_{\mu}(\eta_c)}{P'_{\mu}(-\eta_c)} \frac{P_{\mu}(-\eta_c)}{P_{\mu}(\eta_c)} \simeq \frac{I_1\left(\sqrt{2\delta^{-2}(1-\eta_c)}\right)K_0\left(\sqrt{2\delta^{-2}(1-\eta_c)}\right)}{I_0\left(\sqrt{2\delta^{-2}(1-\eta_c)}\right)K_1\left(\sqrt{2\delta^{-2}(1-\eta_c)}\right)}, \qquad 1 - \eta_c = O(\delta^2), \tag{S31}
$$

which by inspection is a decreasing function of  $\delta^{-2}(1-\eta_c)$  that approaches 0 as  $\delta^{-2}(1-\eta_c) \to$ 0, or 1 as  $\delta^{-2}(1-\eta_c) \to \infty$ . Thus, by Equation [\(S26\)](#page-4-1) we have a unique solution for all  $\gamma$ 

running through the interval  $\gamma \in \left(\frac{2\beta+1}{2(1+2\alpha(\beta+1))}, \frac{\beta+1}{1+2\alpha(\beta+1)}\right)$ , yielding what we call a small spherical cap solution, in which  $\bar{u}(\eta)$  is close to the larger of the two values in Equation [\(S2\)](#page-1-3) in most of the domain, with  $1 - \eta_c = O(\delta^2)$ . Analogously, we alse have a small spherical cap solution for  $\delta \ll 1$  and  $\gamma \in \left(\frac{\beta}{1+2\alpha\beta}, \frac{2\beta+1}{2(1+2\alpha)}\right)$  $\left(\frac{2\beta+1}{2(1+2\alpha\beta)}\right)$ , with  $\bar{u}(\eta)$  taking mostly the smallest of the two values in Equation [\(S2\)](#page-1-3) in most of the domain and with  $1 + \eta_c = O(\delta^2)$ .

#### Linear Stability of Spherical Cap Solutions

We now perform a linear stability analysis of the spherical cap solutions. In our approach we follow [\[2\]](#page-18-1), in which a very similar analysis of radial solutions in balls has been carried out in Sec. 13.2.2 (see also the original Refs. [\[3](#page-18-2)[–5\]](#page-18-3)).

We start by writing Equation (7), using  $(\eta, \phi)$  as independent spatial variables:

$$
\frac{\partial u}{\partial \tau} = -Lu - u + \left(1 - \frac{\alpha}{2\pi} \int_0^{2\pi} \int_{-1}^1 u \, d\eta \, d\phi\right) g_\nu(u),\tag{S32}
$$

where the operator  $L$  and the function  $g$  are defined as

$$
L := -\delta^2 \frac{\partial}{\partial \eta} \left[ (1 - \eta^2) \frac{\partial}{\partial \eta} \right] - \frac{\delta^2}{1 - \eta^2} \frac{\partial^2}{\partial \phi^2}, \qquad g_{\nu}(u) := \beta + \frac{u^{\nu}}{u^{\nu} + \gamma^{\nu}}, \tag{S33}
$$

and linearize this equation around the steady state  $\bar{u} = \bar{u}(\eta)$ , which solves

<span id="page-6-1"></span><span id="page-6-0"></span>
$$
0 = \delta^2 \frac{d}{d\eta} \left[ (1 - \eta^2) \frac{d\bar{u}}{d\eta} \right] - \bar{u} + k g_\nu(\bar{u}), \tag{S34}
$$

where k was defined in Equation [\(S5\)](#page-1-4). Fixing  $m \in \mathbb{Z}$  and  $\lambda_m \in \mathbb{R}$ , substituting

$$
u(\eta, \phi, \tau) = \bar{u}(\eta) + \varepsilon \psi_m(\eta) e^{im\phi - \lambda_m \tau}
$$
 (S35)

into Equation [\(S32\)](#page-6-0) and sending  $\varepsilon \to 0$ , we arrive at the following equation for the eigenmodes  $\psi_m$  and their associated exponential decay/growth rates  $\lambda_m$  (depending on whether  $\lambda_m$  is positive/negative) at leading order in  $\varepsilon$ :

$$
\lambda_m \psi_m = L_m \psi_m + \psi_m - k g'_\nu(\bar{u}) \psi_m + \alpha g_\nu(\bar{u}) \int_{-1}^1 \psi_m(\eta) d\eta, \qquad m = 0,
$$
 (S36)

$$
\lambda_m \psi_m = L_m \psi_m + \psi_m - k g'_\nu(\bar{u}) \psi_m, \qquad m \neq 0, \qquad (S37)
$$

where

$$
L_m := -\delta^2 \frac{d}{d\eta} \left[ (1 - \eta^2) \frac{d}{d\eta} \right] + \frac{\delta^2 m^2}{1 - \eta^2}, \qquad g'(\bar{u}) := \frac{d g_\nu(u)}{d u} \bigg|_{u = \bar{u}}, \tag{S38}
$$

with natural boundary conditions  $\psi_m(\eta) = O\left(|\eta \mp 1|^{\frac{|m|}{2}}\right)$  for  $\eta \to \pm 1$ . Note that in the limit  $\nu \to \infty$  corresponding to the Heaviside function-type nonlinearity  $g_{\infty}(u) = \lim_{\nu \to \infty} g_{\nu}(u) =$  $\beta + H(u - \gamma)$  we recover

$$
g'_{\infty}(\bar{u}(\eta)) = \delta(\eta - \eta_c) \left| \frac{d\bar{u}(\eta_c)}{d\eta} \right|^{-1}, \tag{S39}
$$

where  $\delta(z)$  is the one-dimensional Dirac delta-function.

Let us introduce the Sturm-Liouville operators  $H_m$  and their associated eigenpairs  $(\psi_m^n, \lambda_m^n)$ , which satisfy

$$
H_m \psi_m^n = \lambda_m^n \psi_m^n, \qquad H_m := L_m + 1 - k g'_\nu(\bar{u}), \qquad n = 0, 1, 2, \dots \tag{S40}
$$

According to Sturm-Liouville theory, for each m all eigenvalues  $\lambda_m^0 < \lambda_m^1 < \lambda_m^2 < \cdots \to \infty$ have multiplicity one, and each eigenvalue  $\lambda_m^n$  is associated to an eigenfunction with precisely n zeros in  $(-1, 1)$ . Furthermore, we have  $\lambda_{m'}^0 > \lambda_m^0$  for all  $|m'| > |m| \ge 0$ . The latter can be easily seen from the fact that  $\lambda_m^0$  minimizes the Rayleigh quotient associated with  $H_m$ :

$$
R_m(\psi) := \frac{\int_{-1}^1 \left\{ \delta^2 (1 - \eta^2) |\psi'|^2 + \delta^2 m^2 (1 - \eta^2)^{-1} \psi^2 + \psi^2 - k g'_\nu(\bar{u}) \psi^2 \right\} d\eta}{\int_{-1}^1 \psi^2 d\eta}.
$$
 (S41)

Therefore, we have

$$
\lambda_m^0 = R_m(\psi_m^0) = \min_{\psi} R_m(\psi) \le R_m(\psi_{m'}^0) < R_{m'}(\psi_{m'}^0) = \lambda_{m'}^0,\tag{S42}
$$

where the minimization is carried out over all  $\psi \in W_{loc}^{1,2}(-1,1)$  satisfying  $\int_{-1}^{1} \psi^2 d\eta = 1$ .

We now observe that because of the rotational symmetry of the problem the operators  $H_{\pm 1}$  have a zero eigenvalue associated with the eigenfunction

<span id="page-7-3"></span><span id="page-7-2"></span><span id="page-7-1"></span><span id="page-7-0"></span>
$$
\psi_{\pm 1}^0(\eta) = \sqrt{1 - \eta^2} \frac{d\bar{u}(\eta)}{d\eta}.
$$
\n(S43)

Indeed, differentiating Equation [\(S34\)](#page-6-1) with respect to  $\eta$  and multiplying the resulting equation by  $\sqrt{1 - \eta^2}$ , after some algebra we obtain

$$
0 = -\delta^2 \sqrt{1 - \eta^2} \frac{d^2}{d\eta^2} \left[ (1 - \eta^2) \frac{d\bar{u}}{d\eta} \right] + (1 - k g'_\nu(\bar{u})) \sqrt{1 - \eta^2} \frac{d\bar{u}}{d\eta}
$$

$$
= H_{\pm 1} \left[ \sqrt{1 - \eta^2} \frac{d\bar{u}}{d\eta} \right]. \tag{S44}
$$

Since for the spherical cap solutions the function  $\bar{u}(\eta)$  is strictly monotone decreasing for all  $\eta \in (-1,1)$ , we thus have that  $\sqrt{1 - \eta^2} \frac{d\bar{u}(\eta)}{d\eta}$  does not change sign and is, therefore, the eigenfunction associated with  $\lambda_{\pm 1}^0 = 0$ . This means, in particular, that

$$
\lambda_m^n > 0 \qquad \forall m \neq 0 \text{ and } \forall n \geq 0 \qquad \text{or} \qquad \forall m = \pm 1 \text{ and } \forall n \geq 1. \tag{S45}
$$

It is clear that for  $m \neq 0$  the solutions of the obtained eigenvalue problem are the eigenpairs  $(\psi_m^n, \lambda_m^n)$  of the Sturm-Liouville operator  $H_m$ . Therefore, by Equation [\(S45\)](#page-7-0) all the modes with  $m \neq 0$  are linearly stable, except for the case  $m = \pm 1$  and  $n = 0$  corresponding to infinitesimal rotations, which are neutrally stable. Thus, stability of the spherical cap solutions is determined by the axially symmetric modes corresponding to  $m = 0$ .

Focusing now on the case  $m = 0$ , we first observe that in the absence of the nonlocal term in Equation [\(S32\)](#page-6-0), i.e., when  $\alpha = 0$ , we must have  $\lambda_0^0 < 0$ , in view of Equation [\(S42\)](#page-7-1)

and the fact that  $\lambda_{\pm 1}^0 = 0$ . Therefore, a sufficiently strong global feedback expressed by the integral term in Equation [\(S32\)](#page-6-0) is required for the stability of spherical caps. To proceed with the analysis of  $(\psi_0, \lambda_0)$ , which equivalently satisfy

<span id="page-8-0"></span>
$$
H_0\psi_0 + \alpha g_\nu(\bar{u}) \int_{-1}^1 \psi_0 d\eta = \lambda_0 \psi_0, \qquad (S46)
$$

we note that the operator in the left-hand side of Equation [\(S46\)](#page-8-0) is the Sturm-Liouville operator  $H_0$  plus a rank-one operator (generally, not self-adjoint). Therefore, if any of the eigenfunctions of  $H_0$  satisfy  $\int_{-1}^1 \psi_0^n d\eta = 0$ , then the pair  $(\psi_0^n, \lambda_0^n)$  is also a solution to Equation [\(S46\)](#page-8-0). If not, then according to Fredholm alternative  $\lambda_0^n$  is still an eigenvalue of Equation [\(S46\)](#page-8-0), if  $\int_{-1}^{1} g_{\nu}(\bar{u}) \psi_0^n d\eta = 0$ .

On the other hand, for all  $\lambda_0 \neq \lambda_0^n$  we can rewrite Equation [\(S46\)](#page-8-0) as (see also [\[6\]](#page-18-4))

$$
\psi_0 = -\alpha (H_0 - \lambda_0)^{-1} g_\nu(\bar{u}) \int_{-1}^1 \psi_0 d\eta,
$$
\n(S47)

and integrating the resulting expression yields

<span id="page-8-2"></span><span id="page-8-1"></span>
$$
1 + \alpha \int_{-1}^{1} (H_0 - \lambda_0)^{-1} g_\nu(\bar{u}) d\eta = 0.
$$
 (S48)

We now investigate under which conditions one may have  $\lambda_0 < 0$ , signifying linear instability of the spherical cap solutions. Observe first that  $\lambda_0$  cannot equal  $\lambda_0^0$ , as  $\psi_0^0$  corresponds to the ground state of  $R_0$  and, therefore, has constant sign. On the other hand, for large enough *n* we have  $\lambda_0^n > 0$ , so in order to verify whether the condition

$$
\lambda_0^n < 0
$$
 and  $\int_{-1}^1 \psi_0^n d\eta = 0$  or  $\int_{-1}^1 g_\nu(\bar{u}) \psi_0^n d\eta = 0,$  (S49)

is satisfied for some  $n \geq 1$ , one only needs to verify Equation [\(S49\)](#page-8-1) for finitely many  $n \geq 1$ , if any.

If  $\lambda_0 \neq \lambda_0^n$  for all  $n \geq 0$ , then Equation [\(S48\)](#page-8-2) must be satisfied. To analyze its solutions, we expand its right-hand side with respect to the complete orthogonal basis of the eigenfunctions  $\psi_0^n$  of  $H_0$ :

$$
1 + \alpha \sum_{n=0}^{\infty} \frac{a_n}{\lambda_0^n - \lambda_0} = 0, \qquad a_n := \frac{\int_{-1}^1 \psi_0^n d\eta \int_{-1}^1 g_\nu(\bar{u}) \psi_0^n d\eta}{\int_{-1}^1 |\psi_0^n|^2 d\eta}.
$$
 (S50)

Recall that in this formula  $\lambda_0^0 < 0$ , and we also have  $a_0 > 0$ , since  $\psi_0^0$  has a constant sign.

For  $\omega \in \mathbb{C}$ , defining

<span id="page-8-3"></span>
$$
D(\omega) := 1 + \alpha \sum_{n=0}^{\infty} \frac{a_n}{\lambda_0^n + i\omega},
$$
\n(S51)

we observe that the zeros of  $D(\omega)$  with  $\omega = i\lambda_0$  in the lower half-plane of the complex frequency  $\omega$  would correspond to linearly unstable modes. It is convenient to study the number of zeros of  $D(\omega)$  in the lower-half plane, using the Cauchy argument principle, which states that the number of zeros of this function is equal to

<span id="page-9-0"></span>
$$
N = P + \frac{1}{2\pi} \Delta \arg D(\omega),
$$
 (S52)

where P is the number of poles there and  $\Delta \arg D(\omega)$  is the change of the argument of the function  $D(\omega)$  as  $\omega$  runs from  $+\infty$  to  $-\infty$  along the real axis. Thus, the number of negative eigenvalues of  $H_0$  and the winding number of arg  $D(\omega)$  ultimately encode the stability of the solution.

The analysis of Equation [\(S52\)](#page-9-0) requires the precise information on the spectrum of  $H_0$ and the magnitudes of  $a_n$  (for an example of an analytical treatment in a related context, see [\[7\]](#page-18-5)). For  $\nu = \infty$  this problem may once again be treated with the help of the Legendre functions, similarly to the way we constructed the spherical cap solutions. It is not diffucult to see that in this case the eigenfunctions of  $H_0$  normalized to equal 1 at  $\eta = \eta_c$  must satisfy

$$
\psi_0^n(\eta) = \begin{cases} \frac{P_{\mu_0^n}(-\eta)}{P_{\mu_0^n}(-\eta_c)} & -1 < \eta < \eta_c, \\ \frac{P_{\mu_0^n}(\eta)}{P_{\mu_0^n}(\eta_c)} & \eta_c < \eta < 1, \end{cases} \qquad \mu_0^n := -\frac{1}{2} + \frac{1}{2} \sqrt{1 - \frac{4(1 - \lambda_0^n)}{\delta^2}}, \qquad (S53)
$$

assuming  $P_{\mu_0^n}(\pm \eta_c) \neq 0$ . In turn, the eigenvalues  $\lambda_0^n$  are obtained from the solution of the algebraic equation

$$
\frac{\delta^2 (1 - \eta_c^2)}{k} \left| \frac{d\bar{u}(\eta_c)}{d\eta} \right| \left( \frac{P'_{\mu_0^n}(\eta_c)}{P_{\mu_0^n}(\eta_c)} + \frac{P'_{\mu_0^n}(-\eta_c)}{P_{\mu_0^n}(-\eta_c)} \right) = -1,
$$
\n(S54)

where k is defined in Equation [\(S17\)](#page-3-8) and  $\frac{d\bar{u}(\eta_c)}{d\eta}$  is obtained by differentiating  $\bar{u}(\eta)$  from Equation [\(S15\)](#page-3-0) and setting  $\eta = \eta_c$ . Equation [\(S54\)](#page-9-1) is obtained by matching the jump of the derivative of  $\psi_0^n(\eta)$  at  $\eta = \eta_c$  due to the delta-function in the definition of  $H_0$ .

To get some physical insight into instability we may observe that the coefficients  $a_n$  in Equation [\(S50\)](#page-8-3) are expected to be rapidly decreasing with n, while  $\lambda_0^n$  are, in turn, rapidly increasing in n. Therefore, it may not be unreasonable to approximate the function  $D(\omega)$ by keeping only the first term in the series [\[2\]](#page-18-1). We would then arrive at the expression

<span id="page-9-1"></span>
$$
D(\omega) \approx 1 - \frac{\alpha a_0}{|\lambda_0^0| - i\omega},\tag{S55}
$$

where we explicitly took into account that  $\lambda_0^0 < 0$ . For this choice of  $D(\omega)$  we can conclude that  $P = 1$  and the image of  $D(\omega)$  is a simple closed contour oriented clockwise. Thus, whether  $D(\omega)$  has a zero in the lower half-plane depends on whether or not this contour encloses the origin. Checking the sign of  $D(0)$ , we then arrive at an approximate instability criterion:

<span id="page-9-2"></span>
$$
\alpha \lesssim \frac{|\lambda_0^0|}{a_0}.\tag{S56}
$$

As expected, all spherical cap solutions should be unstable for all sufficiently small  $\alpha$ , while stability may be achieved for sufficiently large values of  $\alpha$ . For a representative set of parameters  $(\alpha, \beta, \gamma, \delta) = (1, 0, 0.28, 0.4)$  corresponding to a large spherical cap, solving Equa-tion [\(S54\)](#page-9-1) numerically yields  $\{\lambda_0^n\}_{n=0}^4 = \{-0.216, 1.228, 1.798, 2.513, 4.187\}$ , and corresponding  ${a_n}_{n=0}^4 = {0.545, -0.142, 0.195, 0.010, -0.005}.$  Keeping only  $\lambda_0^0$  and  $a_0$ , we get the bound for instability  $\alpha < 0.396$ , while the bound for instability from using these first five terms gives  $\alpha < 0.395$ , in excellent agreement with the heuristics provided before Equation [\(S56\)](#page-9-2). In particular, the solution for these values of the parameters is linearly stable.

One can give a more precise argument for stability of large spherical caps (i.e., those for which the value of  $\eta = \eta_c$  at which the threshold  $\gamma = \bar{u}(\eta_c)$  is reached, see Equation [\(S26\)](#page-4-1), is not too close to  $\eta = \pm 1$ ) in the case  $\nu = \infty$  and  $\delta \ll 1$ . First of all, in the case of the Heaviside nonlinearity the operator  $H_0$  has exactly one negative eigenvalue. In fact, it is not difficult to see that all  $\lambda_0^n > 1$  for  $n \geq 1$  in this case. Indeed, introduce a change of variables

<span id="page-10-0"></span>
$$
\eta = \tanh z, \qquad z \in (-\infty, +\infty). \tag{S57}
$$

Then the equation for the eigenfunctions of  $H_0$  becomes (with a slight abuse of notation, using the same letters to denote the corresponding functions of  $z$ )

$$
-\delta^2 \frac{d^2 \psi_0^n}{dz^2} + \cosh^{-2} z \left(1 - k \left| \frac{d\bar{u}(z_c)}{dz} \right|^{-1} \delta(z - z_c) \right) \psi_0^n = \lambda_0^n \psi_0^n \cosh^{-2} z,\tag{S58}
$$

where  $z_c \in \mathbb{R}$  is such that  $\eta_c = \tanh z_c$ .

Consider now  $\psi_0^n(z)$  with  $n \geq 1$ , and without loss of generality assume that  $\psi_0^n(z_0) = 0$ for some  $z_0 \geq z_c$ , and that  $d\psi_0^n(z_0)/dz > 0$ . Then if  $\lambda_0^n \leq 1$ , the function  $\psi_0^n$  satisfies

$$
\frac{d^2\psi_0^n(z)}{dz^2} = (1 - \lambda_0^n)\delta^{-2}\psi_0^n(z)\cosh^{-2} z \ge 0 \qquad \forall z \in (z_0, +\infty). \tag{S59}
$$

Thus,  $\psi_0^n(z) \ge C(z - z_0)$  for some  $C > 0$  and, therefore, we have  $\psi_0^n(z) \to \infty$  as  $z \to +\infty$ , contradicting boundedness of the eigenfunctions of  $H_0$  for any  $n \geq 1$ .

We thus established that for  $\nu = \infty$  we have  $P = 1$  in Equation [\(S52\)](#page-9-0). Next we note that for  $\delta \ll 1$  the eigenvalues of  $H_0$  behave as  $\lambda_0^n - 1 \sim n^2 \delta^2$  for  $n \ge 1$ . This allows us to use a local approximation

$$
\sum_{n=1}^{\infty} \frac{a_n}{\lambda_0^n + i\omega} \simeq \frac{a_{\infty} - a_0}{1 + i\omega}, \qquad a_{\infty} := \int_{-1}^1 g_{\infty}(\bar{u}) d\eta,
$$
 (S60)

in the case  $\delta \ll 1$ , which is obtained by replacing  $\lambda_0^n$  in Equation [\(S50\)](#page-8-3) with 1 and using completeness of the family  $(\psi_0^n)_{n=0}^{\infty}$ . Putting everything together yields

$$
D(\omega) \simeq 1 - \alpha \left( \frac{a_0}{|\lambda_0^0| - i\omega} + \frac{a_0}{1 + i\omega} - \frac{a_\infty}{1 + i\omega} \right). \tag{S61}
$$

To conclude, we observe that as  $\delta \to 0$  we have

<span id="page-10-1"></span>
$$
a_0 = O(\delta) \qquad \text{and} \qquad \lambda_0^0 = O(\delta^2). \tag{S62}
$$

To see this, write the equation for  $\bar{u} = \bar{u}(z)$ :

$$
0 = \delta^2 \frac{d^2 \bar{u}}{dz^2} - (\bar{u} - k g_{\infty}(\bar{u})) \cosh^{-2} z, \qquad g_{\infty}(\bar{u}(z)) = \beta + H(z_c - z). \tag{S63}
$$

Solving Equation [\(S63\)](#page-11-0) to the leading order in  $\delta \ll 1$ , we obtain

$$
\bar{u}(z) \simeq \begin{cases} k\beta + \frac{1}{2}ke^{-\frac{z-z_c}{\delta\cosh z_c}}, & z \ge z_c, \\ k(\beta + 1) - \frac{1}{2}ke^{-\frac{z_c - z}{\delta\cosh z_c}}, & z < z_c. \end{cases}
$$
(S64)

In particular, we have

<span id="page-11-1"></span><span id="page-11-0"></span>
$$
\frac{d\bar{u}(z)}{dz} \simeq -\frac{k}{2\delta \cosh z_c} e^{-\frac{|z-z_c|}{\delta \cosh z_c}}.\tag{S65}
$$

Similarly, Equation [\(S58\)](#page-10-0) with  $n = 0$  is

$$
-\delta^2 \frac{d^2 \psi_0^0}{dz^2} + \cosh^{-2} z \left(1 - k \left| \frac{d\bar{u}(z_c)}{dz} \right|^{-1} \delta(z - z_c) \right) \psi_0^0 = \lambda_0^0 \psi_0^0 \cosh^{-2} z,
$$
 (S66)

and its solution to the leading order in  $\delta \ll 1$ , corresponding to  $\lambda_0^0 \simeq 0$  to  $O(\delta)$ , is explicitly

<span id="page-11-6"></span><span id="page-11-4"></span><span id="page-11-3"></span>
$$
\psi_0^0(z) \simeq \frac{d\bar{u}(z)}{dz},\tag{S67}
$$

noting that  $d\bar{u}(z)/dz$  from Equation [\(S65\)](#page-11-1) does not change sign. Substituting this expression, after a suitable normalization, into the definition of  $a_0$  in Equation [\(S50\)](#page-8-3), we obtain, again to the leading order in  $\delta \ll 1$ :

<span id="page-11-2"></span>
$$
a_0 \simeq 2\delta(2\beta + 1)\sqrt{1 - \eta_c^2},\tag{S68}
$$

where we took into account that  $\cosh^{-2} z_c = 1 - \eta_c^2$ .

At the same time, by Equation [\(S44\)](#page-7-2) we have

$$
-\delta^2 \frac{d^2 \psi_{\pm 1}^0}{dz^2} + \delta^2 \psi_{\pm 1}^0 + \cosh^{-2} z \left(1 - k \left| \frac{d\bar{u}(z_c)}{dz} \right|^{-1} \delta(z - z_c) \right) \psi_{\pm 1}^0 = 0. \tag{S69}
$$

Therefore, to the leading order in  $\delta \ll 1$  we obtain from Equation [\(S43\)](#page-7-3):

<span id="page-11-5"></span>
$$
\psi_{\pm 1}^0(z) \simeq \cosh^{-1} z_c \frac{d\bar{u}(z)}{dz}.\tag{S70}
$$

We now multiply Equation [\(S69\)](#page-11-2) by  $\psi_0^0$  and integrate over the real line. Likewise, we multiply Equation [\(S66\)](#page-11-3) by  $\psi_{\pm 1}^0$  and integrate. Subtracting the obtained results yields

$$
\delta^2 \int_{-\infty}^{\infty} \psi_0^0 \psi_{\pm 1}^0 dz = -\lambda_0^0 \int_{-\infty}^{\infty} \psi_0^0 \psi_{\pm 1}^0 \cosh^{-2} z \, dz. \tag{S71}
$$

Thus, to the leading order in  $\delta \ll 1$  we have, with the help of Equation [\(S67\)](#page-11-4) and Equation [\(S70\)](#page-11-5):

<span id="page-12-0"></span>
$$
\lambda_0^0 \simeq -\frac{\delta^2}{1 - \eta_c^2},\tag{S72}
$$

where we again used the fact that  $\cosh^{-2} z_c = 1 - \eta_c^2$ .

Finally, since by the definition in Equation [\(S60\)](#page-10-1) we have

$$
a_{\infty} = 2\beta + \eta_c + 1,\tag{S73}
$$

and, hence,  $a_{\infty} = O(1)$  as  $\delta \to 0$ , we may conclude by inspection of

$$
D(\omega) \simeq 1 - \frac{\alpha a_0 |\lambda_0^0|}{|\lambda_0^0|^2 + \omega^2} + \frac{\alpha (a_\infty - a_0)}{1 + \omega^2} - i\alpha \omega \left(\frac{a_0}{|\lambda_0^0|^2 + \omega^2} + \frac{a_\infty - a_0}{1 + \omega^2}\right),
$$
 (S74)

that  $\omega \text{Im } D(\omega) < 0$  and  $D(0) < 0$  for all  $\delta \ll 1$  and  $\eta_c \in (-1,1)$  fixed. Therefore, in this case  $\Delta \arg D(\omega) = -2\pi$ , and by Equation [\(S52\)](#page-9-0) there are no negative eigenvalues for large spherical caps in the limit  $\delta \to 0$ . In other words, large spherical caps are always linearly stable for  $\delta \ll 1$ ,  $1 - \eta_c^2 = O(1)$  and  $\alpha = O(1)$ . More precisely, for  $\delta \ll 1$  and  $\eta_c$  not approaching  $\pm 1$  a spherical cap solution is linearly stable if and only if

$$
\alpha > \alpha_c, \qquad \alpha_c \simeq \frac{\delta}{2(2\beta + 1)(1 - \eta_c^2)^{3/2}}.\tag{S75}
$$

where the asymptotic value of  $\alpha_c$  is obtained by setting  $D(0) = 0$ , to the leading order in  $\delta \ll 1$ , and using the asymptotic expressions in Equation [\(S68\)](#page-11-6) and Equation [\(S72\)](#page-12-0). The instability is a consequence of Equation [\(S52\)](#page-9-0) and the fact that  $\Delta \arg D(\omega) = 0$  when  $D(0) > 0$ . Notice that by Equation [\(S28\)](#page-4-2) at  $\alpha = O(\delta)$  the large cap solution exists only in a narrow range of values of  $\gamma$  of width  $O(\delta)$ . At the same time, when  $\alpha \gg 1$ , the range of  $\gamma$  for existence narrows again to  $O(\alpha^{-1})$ , unless  $\beta \lesssim \alpha^{-1}$ . Lastly, it is easy to see that for small cap solutions one should expect  $|\lambda_0^0| = O(1)$  and  $a_0 = O(\delta^2)$ , since for those solutions  $\bar{u}(\eta)$  is close to constant, unless  $1 - \eta^2 = O(\delta^2)$ . Therefore, by the previous arguments the small spherical cap solutions are always unstable for  $\delta \ll 1$ .

#### Estimating Spatial Variation of Cytoplasmic Component

We now examine under which conditions the approximation of constant concentration of the species on the cell membrane used to derive Equation (7) in the main body of the paper is reasonable. To this end, we estimate the relative deviation of the concentration C on  $\partial\Omega$ from its average C by solving Equations  $(1)$ –(3) at steady state with a prescribed steady state profile of the membrane bound species  $B$ . Notice that since  $C$  solves the Laplace's equation in  $\Omega$ , we have that  $\overline{C}$  is also the average value of C in  $\Omega$ .

We expand the solution  $C = C(\rho, \theta, \phi)$  of Equation (1) written in spherical coordinates, using spherical harmonics  $Y_l^m$  in  $\Omega$ :

$$
C(\rho, \theta, \phi) = \sum_{l=0}^{\infty} \sum_{m=-l}^{l} C_l^m (\rho/r)^l Y_l^m(\theta, \phi).
$$
 (S76)

From this formula, we have that the normal flux appearing in the left-hand side of Equation (3), as well as the solution itself on  $\partial\Omega$  may be written as

$$
D_C(n \cdot \nabla C)|_{\partial \Omega} = D_C \sum_{l=0}^{\infty} \sum_{m=-l}^{l} lr^{-1} C_l^m Y_l^m(\theta, \phi), \qquad C|_{\partial \Omega} = \sum_{l=0}^{\infty} \sum_{m=-l}^{l} C_l^m Y_l^m(\theta, \phi). \quad (S77)
$$

On the other hand, we can also write the following expansions for B and  $-\Delta_{\partial\Omega}B$  on  $\partial\Omega$ :

$$
B(\theta,\phi) = \sum_{l=0}^{\infty} \sum_{m=-l}^{l} B_l^m Y_l^m(\theta,\phi), \qquad -\Delta_{\partial\Omega} B(\theta,\phi) = \sum_{l=0}^{\infty} \sum_{m=-l}^{l} l(l+1) r^{-2} B_l^m Y_l^m(\theta,\phi).
$$
\n(S78)

Noting that by Equations (1) and (3) at steady state we have  $D_C(n \cdot \nabla C)|_{\partial \Omega} = D_B \Delta_{\partial \Omega} B$ , from the above two equations we can see that for all  $l \neq 0$  we have

$$
D_C C_l^m = -D_B (l+1) r^{-1} B_l^m,
$$
\n(S79)

and, therefore, there holds

$$
D_C^2 \sum_{l=1}^{\infty} \sum_{m=-l}^{l} |C_l^m|^2 = \frac{D_B^2}{r^2} \sum_{l=1}^{\infty} \sum_{m=-l}^{l} (l+1)^2 |B_l^m|^2 \le \frac{2D_B^2}{r^2} \sum_{l=1}^{\infty} \sum_{m=-l}^{l} l(l+1) |B_l^m|^2. \tag{S80}
$$

Thus, from Parseval's identity and integration by parts we obtain

$$
D_C^2 \int_0^{2\pi} \int_0^{\pi} |C(r,\theta,\phi) - \bar{C}|^2 \sin\theta \,d\theta \,d\phi \le -\frac{2D_B^2}{r^2} \int_0^{2\pi} \int_0^{\pi} B(\theta,\phi) \Delta_{\mathbb{S}^2} B(\theta,\phi) \sin\theta \,d\theta \,d\phi
$$

$$
= \frac{2D_B^2}{r^2} \int_0^{2\pi} \int_0^{\pi} |\nabla_{\mathbb{S}^2} B(\theta,\phi)|^2 \sin\theta \,d\theta \,d\phi. \tag{S81}
$$

Thus, we have found that on average the relative deviation of the concentration C on the cell membrane from its average value  $\overline{C}$  in the cytosol is

$$
\sqrt{\left\langle \left(\frac{C-\bar{C}}{\bar{C}}\right)^2 \right\rangle_{\partial\Omega}} = \sqrt{\int_{\partial\Omega} \frac{|C-\bar{C}|^2}{4\pi r^2 \bar{C}^2} dA} \le \frac{D_B \max B}{D_C \bar{C}r} \sqrt{\frac{1}{2\pi \max B^2} \int_{\partial\Omega} |\nabla B|^2 dA}.
$$
 (S82)

Notice that apart from the expression inside the square root in the right-hand side of Equation [\(S82\)](#page-13-0), which is scale-free and thus only weakly depends on the solution for B (for example, this expression is bounded by  $1/4$  when B is an exponentially decaying profile as a function of  $\theta$ ), the left-hand side of Equation [\(S82\)](#page-13-0) is controlled by

<span id="page-13-1"></span><span id="page-13-0"></span>
$$
\sqrt{\left\langle \left(\frac{C-\bar{C}}{\bar{C}}\right)^2 \right\rangle_{\partial\Omega}} \le \frac{MD_B N_B}{3D_C N_C},\tag{S83}
$$

where  $N_B = 4\pi r^2 \max B$  is the maximum number of molecules that can be bound to the cell membrane,  $N_C = \frac{4}{3}$  $\frac{4}{3}\pi r^3 \bar{C}$  is the number of molecules in the cytosol, and M is the solution profile shape factor given by the square root in the right-hand side of Equation [\(S82\)](#page-13-0) and expected to be of order unity. Thus, neglecting the variations of C across the cell membrane is justified whenever the surface diffusion is much slower than the bulk diffusion, as well as when the number of membrane bound molecules is smaller than that in the bulk. Using  $[8]$ , we have  $D_B = 0.03 \ \mu m^2 s^{-1}$ ,  $D_C = 11 \ \mu m^2 s^{-1}$ ,  $k_b = 0.28 \ \mu m s^{-1}$ ,  $k_d = 1 \ s^{-1}$ ,  $C_0 =$ 11.621  $\mu$ m<sup>-3</sup>, and  $r = 3.95 \mu$ m. An appropriate choice of Γ to produce a spherical cap gives  $N_B = 643$ ,  $N_C = 2749$ , and  $M = 1.523$ , which gives an upper bound of  $3.24 \times 10^{-4}$  for the left-hand side in Equation [\(S83\)](#page-13-1), which is clearly negligible. Of course, in reality the estimate in [\(S83\)](#page-13-1) is fairly conservative, and so in practice neglecting the variations of C should always provide a very good approximation.

#### Parametric Analysis of Localized Patterns

Recall the five dimensionless groups defined in Equation (7) of the main text:

$$
\alpha := \frac{3}{2} \frac{k_b}{k_d r}, \quad \gamma := \frac{k_d \Gamma}{k_b C_0}, \quad \delta := \frac{1}{r} \sqrt{\frac{D_B}{k_d}}, \quad \nu, \text{ and } \beta.
$$

Here, we analyze how perturbations with respect to various biological and kinetic parameters affect the formation of the stable spherical cap. Because  $\beta$  has no functional dependence on any other biological parameters within the system, we shall only consider the relationships between  $\alpha, \gamma$ , and  $\delta$  for  $\nu \to \infty$  in this section.

In this regime, we have demonstrated that the four remaining dimensionless groups satisfy Equation (11) of the main text when a stable spherical cap may be formed. Thus, by fixing one of  $\alpha, \gamma$ , or  $\delta$  and keeping  $\beta$  constant, we may draw two-dimensional curves that define the edge of stability for spherical cap solutions, as shown in Figure [S2.](#page-15-0) Using the definitions of these dimensionless groups, we may observe the effects of varying different constants.

The biological parameters  $\Gamma$  and  $C_0$  only appear as terms in the definition of  $\gamma$ . Therefore, perturbing these cellular properties has the effect of changing  $\gamma$  only, with no effect on  $\alpha$  or  $\delta$ . As can be seen in Figure 3B of the main text, for a large enough perturbation of  $\gamma$  in either direction, a system that initial allows for polarization may leave the domain of stability and eventually only yield a homogeneous steady state. In a similar way,  $D_B$  only affects  $\delta$ , but it can be seen that only a sufficient increase in  $D_B$  may cause stable steady state solutions to become unstable.

As both  $\alpha$  and  $\delta$  are proportional to  $1/r$ , increasing and decreasing the radius can induce instability for cap-like solutions, as shown in Figure [S2.](#page-15-0) Because the effect on  $\gamma$  of decreasing  $k_b$  is the inverse of its effect on  $\alpha$ , Figure [S2](#page-15-0) highlights that polarization will eventually disappear. However, increasing  $k_b$  appears to only have this effect for polarizable systems with small  $\alpha$  and large  $\gamma$ ; outside this regime, the system remains stable as it approaches an asymptote along the edge of stability. A similar effect can be seen by changing  $k_d$ . However, in this case, all dimensionless groups are affected by its variation.

#### Analytical Computations

Given a set of parameters  $(\alpha, \beta, \gamma, \delta)$ ,  $u(\eta)$ , the axisymmetric steady state spherical cap



<span id="page-15-0"></span>Figure S2: Left: *Bifurcation diagram of*  $\delta$  *vs.*  $\alpha$  *for*  $\beta = 0.1, \gamma = 0.375$ . The dashed line represents the change in  $\alpha$  and  $\delta$  as cell radius is varied. For the symmetry breaking quadruple  $(\alpha, \beta, \gamma, \delta) = (0.5, 0.1, 0.375, 0.3),$  both increasing or decreasing the cell radius eventually results in a loss of stable cap solution. Right: Bifurcation diagram of  $\gamma^{-1}$  vs.  $\alpha$  for  $\beta =$ 0.1,  $\delta = 0.3$ . Here, the dashed lines highlight the dependence of  $\alpha$  and  $\gamma$  with respect to the binding rate constant  $k_b$ .

profile originating from  $\eta = -1$ , may be plotted by using Equations (9)-(10) of the main text. Here, the LegendreP[,] function in Mathematica is used to calculate both  $u(\eta)$  and the  $\gamma(\eta_c)$  profile described by Equation 11 of the main text.

Equation (11) defines a region in the parameter space of  $(\alpha, \beta, \gamma, \delta)$  where spherical cap solutions are stable steady states. Here, one may plot  $\gamma$  as a function of  $\alpha, \beta$ , and  $\delta$  for  $\eta_c \in (-1, 1)$  to observe its behavior. For sufficiently large  $\delta$  at a given  $\alpha$  and  $\beta$ , this function becomes monotonically increasing in the domain of  $\eta_c$ . For some fixed value of  $\gamma = \gamma^*$ , the equation  $\gamma(\eta_c) - \gamma^* = 0$  will have only one root, corresponding to one value of  $\eta_c$  that gives a symmetry broken solution under this parameter set. This solution must be unstable by the heuristic identified in the main text; if  $\gamma^*$  is increased under these conditions, the profile would suggest a larger value of  $\eta_c$  satisfies the root of the equation, corresponding to a larger cap. If  $\gamma$  is the threshold by which patterns may form, increasing the value for  $\gamma$  should intuitively decrease the possible cap size, implying the original solution corresponded to an unstable pattern. Thus, stable patterns are restricted to locally decreasing regions of  $\gamma(\eta_c)$ in the domain  $\eta_c \in (-1,1)$ .

As  $\delta$  decreases, the  $\gamma$  profile becomes N-shaped, suggesting the existence of a critical value of  $\delta$  where  $\gamma(\eta_c)$  loses its monotonicity, with some  $\eta_c < 0$  yielding a local maximum for  $\gamma(\eta_c)$  and some  $\eta_c > 0$  yielding a local minimum. For a given set of  $(\alpha, \beta, \delta)$  where  $\gamma(\eta_c)$ exhibits cubic-like behavior, the D[,] and FindRoot[] functions in Mathematica allow for the value of  $\eta_c$  to be found that correspond to the maximum and minimum. Direct calculation of  $\gamma$  for each  $\delta$  at these points form the edge of stability for spherical caps at fixed  $\alpha$  and  $\beta$ . Connecting these points creates a cusp-like region in parameter space, as shown in Figure  $3B$  of the main text. This process bounds the region where stable spherical caps may form, and for a set of parameters  $(\alpha, \beta, \gamma, \delta)$ , one can identify whether polarization is possible.

#### Numerical Analysis with Chebfun

The PDE from Equation (7) in the main text is a standard semi-linear PDE of the form

$$
\frac{\partial u}{\partial \tau} = \delta^2 \nabla_{\mathbb{S}^2}^2 u + \mathcal{N}(u),\tag{S84}
$$

with the nonlinear operator  $\mathcal{N}(u)$  given by:

$$
\mathcal{N}(u) = \left(1 - \frac{\alpha}{2\pi} \int_0^{2\pi} \int_0^{\pi} u \sin \theta \, d\theta \, d\phi\right) (\beta + H(u - \gamma)) - u. \tag{S85}
$$

To solve PDEs of this form, the Double Fourier Sphere (DFS) method is used in space [\[9\]](#page-19-1) and an implicit-explicit algorithm is used in time. The DFS method is based on two-dimensional (2D) truncated Fourier series,

<span id="page-16-0"></span>
$$
u(t, \phi, \theta) \approx \sum_{j=-m/2}^{m/2} \sum_{k=-n/2}^{n/2} \hat{u}_{jk}(t) \exp(i(j\theta + k\phi)),
$$
 (S86)

on an equidistant  $n \times m$  longitude-latitude grid, where the primes on the summation signs indicate that the boundary terms  $j = \pm m/2$  and  $k = \pm n/2$  are halved. When Equation [\(S86\)](#page-16-0) is substituted into the general semi-linear form of the PDE, a system of nm ODEs for the Fourier coefficients  $\hat{u}_{jk}(t)$  given by  $\hat{u}' = \delta^2 \mathbf{L} \hat{u} + \mathbf{N}(\hat{u})$  is obtained, where **L** (a nm × nm matrix) and N are the discretized versions of  $\nabla_{\mathbb{S}^2}^2$  and N, respectively. L is a block-diagonal matrix with banded blocks and may be inverted in  $\mathcal{O}(mn)$  operations. The nonlinear operator N can be decomposed as  $\mathbf{N}(\hat{u}) = \mathbf{N}_1(\hat{u})\mathbf{N}_2(\hat{u}) - \hat{u}$ , where  $\mathbf{N}_1$  and  $\mathbf{N}_2$  are given by:

$$
\mathbf{N}_1(\hat{u}) = 1 - \frac{\alpha}{2\pi} \int_0^{2\pi} \int_0^{\pi} u \sin\theta \, d\theta \, d\phi \approx 1 - \alpha \sum_{j=-m/2}^{m/2-1} \hat{u}_{j0}(t) \frac{1 + \exp(i j \pi)}{1 - j^2},
$$
(S87)

<span id="page-16-1"></span>
$$
\mathbf{N}_2(\hat{u}) = \mathbf{F}(\beta + H(\mathbf{F}^{-1}\hat{u} - \gamma)),\tag{S88}
$$

where **F** denotes the 2D fast Fourier transform (FFT). Here, the standard implicit-explicit IMEX-BDF4 scheme is used for time-stepping:

$$
(25\mathbf{I}_{nm} - 12h\mathbf{L})\hat{u}^{n+1} = 48\hat{u}^n - 36\hat{u}^{n-1} + 16\hat{u}^{n-2} - 3\hat{u}^{n-3} + 48h\mathbf{N}(\hat{u}^n) - 72h\mathbf{N}(\hat{u}^{n-1}) + 48h\mathbf{N}(\hat{u}^{n-2}) - 12h\mathbf{N}(\hat{u}^{n-3}),
$$
 (S89)

with time-step h and  $\hat{u}^n = \hat{u}(t_n)$ . At each time-step, a linear system is solved to obtain the Fourier coefficients  $\hat{u}^{n+1}$  at linear cost. Therefore, the dominant cost in Equation [\(S89\)](#page-16-1) is the  $\mathcal{O}(mn \log mn)$  2D FFT for the nonlinear evaluations. Because this is a multi-step formula, it must be started with a one-step scheme. In this case, we use the LIRK4 algorithm.

As a test case, we solved the problem with the following parameters:  $\alpha = 1, \beta = 0.1,$ 

 $\gamma = 0.3$  and  $\delta^2 = 0.05$ , with the initial condition  $u(t = 0, x, y, z) = \exp(-2(x^2 + y^2 + (z - 1)^2))$ , up to  $\tau = 50$ . Here, we used the time-step  $h = 0.1$  over various grid sizes  $m = n$ , with a smooth approximation of the Heaviside function,  $H(x) \approx (1 + \exp(-2\mu x))^{-1}$  where  $\mu =$  $m/(5 \log m)$ . The exact solution at steady state was found analytically through substitution into Equations (9)-(10) of the main text. We then computed the relative  $L^2$ -error between exact and computed solutions as a function of the number of grid points. In this case, we obtained a nearly quadratic convergence in space (see Figure [S3\)](#page-17-0).



<span id="page-17-0"></span>Figure S3: Relative  $L^2$ -error between exact and computed solutions. The convergence is quadratic in space (up to logarithmic factors).

Following [\[10\]](#page-19-2), independent, normally distributed initial conditions are obtained by truncated spherical harmonic expansions with normalized, random coefficients  $c_{\ell,j} \sim \mathcal{N}(0, 1)$ , given by:

$$
u(t = 0, \phi, \theta) = \sum_{\ell=0}^{m} \sum_{j=-\ell}^{\ell} c_{\ell,j} Y_{\ell,j}(\phi, \theta) = \sum_{\ell=0}^{m} \sum_{j=-\ell}^{\ell} c_{\ell,j} P_{\ell}^{j}(\cos \theta) \exp(i j \phi), \quad (S90)
$$

for  $Y_{\ell,j}$ , the spherical harmonic of degree  $\ell$  and order j and  $P_{\ell}^{j}$  $\ell^j$ , the (normalized) associated Legendre polynomial. Functions of maximum wavelength,  $\lambda$ , are obtained for  $m = 2\pi/\lambda$ . All values for  $u(t = 0, \phi, \theta)$  are then scaled appropriately so they are non-negative have a mean less than  $1/(2\alpha)$ .

#### Localization of Spherical Cap by Convection

The effect of cortical flows was modeled by adding a new term to the equation for the membrane species:

$$
\frac{\partial B}{\partial t} = D_B \nabla_{rS^2}^2 B - \nabla \cdot (\mathbf{v}B) + k_b \left( \beta + \frac{B^\nu}{B^\nu + \Gamma^\nu} \right) C - k_d B,\tag{S91}
$$

where  $\mathbf{v} = (\mathbf{v}_{\theta}, \mathbf{v}_{\phi})$  is some predefined velocity field with azimuthal and polar components  $\mathbf{v}_{\theta}$ and  $\mathbf{v}_{\phi}$ , respectively. We considered a unidirectional profile  $\mathbf{v}_{\theta} = \xi \sin \theta$  and  $\mathbf{v}_{\phi} = 0$ , where  $\xi$ is a constant. This flow profile is strongest near the equator and vanishes near the poles. In the regime of fast cytoplasmic diffusion, this leads to the modified version of Equation (7):

$$
\frac{\partial u}{\partial \tau} = \delta^2 \left( \frac{1}{\sin \theta} \frac{\partial}{\partial \theta} \left( \sin \theta \frac{\partial u}{\partial \theta} \right) + \frac{1}{\sin^2 \theta} \frac{\partial^2 u}{\partial \phi^2} \right) - \frac{\epsilon}{\sin \theta} \frac{\partial (u \sin^2 \theta)}{\partial \theta} \n+ \left( 1 - \frac{\alpha}{2\pi} \int_0^{2\pi} \int_0^{\pi} u \sin \theta \, d\theta \, d\phi \right) \left( \beta + \frac{u^{\nu}}{u^{\nu} + \gamma^{\nu}} \right) - u.
$$
\n(S92)

The new dimensionless group,  $\epsilon \equiv \xi/(k_d r)$ , can be interpreted as the ratio of the time scale of dissociation from the membrane and the time scale of convective transport along the surface. Transient flow that is present only during the finite time window  $\tau \in [0, \tau_c]$  is modeled by multiplying the new term by a Heaviside function:

<span id="page-18-6"></span>
$$
\frac{\partial u}{\partial \tau} = \delta^2 \left( \frac{1}{\sin \theta} \frac{\partial}{\partial \theta} \left( \sin \theta \frac{\partial u}{\partial \theta} \right) + \frac{1}{\sin^2 \theta} \frac{\partial^2 u}{\partial \phi^2} \right) - \frac{\epsilon}{\sin \theta} \frac{\partial (u \sin^2 \theta)}{\partial \theta} H(\tau_c - \tau) + \left( 1 - \frac{\alpha}{2\pi} \int_0^{2\pi} \int_0^{\pi} u \sin \theta \, d\theta \, d\phi \right) \left( \beta + \frac{u^{\nu}}{u^{\nu} + \gamma^{\nu}} \right) - u.
$$
 (S93)

Equation [\(S93\)](#page-18-6) was solved using Chebfun, as described above. In Figure 4 of the main text, the spherical cap was formed for  $\epsilon = 1$  and  $\tau_c = 2$  from an initially homogeneous profile, with  $(\alpha, \beta, \gamma, \delta^2) = (1, 0.1, 0.35, 0.05)$  in the regime  $\nu \gg 1$ .

#### Supporting References

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