

A Non-dimensionalization

Here we non-dimensionalize (2.2) to obtain the PDE-ODE system (2.3). Let $[z]$ denote the unit of some variable z . In the SI unit system, we have

$$\begin{aligned} [U] &= \frac{\text{moles}}{\text{m}^2}, & [DU] &= \frac{\text{m}^2}{\text{s}}, & [\kappa_U] &= \frac{1}{\text{s}}, & [T] &= \text{s}, & [X] &= \text{m}, \\ [M_j] &= \text{moles}, & [\kappa_R] &= \frac{1}{\text{s}}, & [\mu_c] &= \text{moles}, & [\beta_{U,1}] &= \frac{\text{m}}{\text{s}}, & [\beta_{U,2}] &= \frac{1}{\text{ms}}. \end{aligned}$$

Letting L denote the length-scale of the domain, we introduce the dimensionless variables $u \equiv L^2U/\mu_c$, $v \equiv L^2V/\mu_c$, $t \equiv \kappa_R T$, $\mathbf{x} \equiv X/L$, $\mu_j \equiv M_j/\mu_c$, and $\eta_j \equiv H_j/\mu_c$. Then, we obtain that

$$\begin{aligned} \kappa_R \partial_t U &= \frac{D_U}{L^2} \Delta_{\mathbf{x}} U - \kappa_U U, & \Leftrightarrow & & \partial_t u &= D_u \Delta_{\mathbf{x}} u - \sigma_u u, & \mathbf{x} &\in \Omega \setminus \bigcup_{j=1}^m \Omega_j, \\ \kappa_R \partial_t V &= \frac{D_V}{L^2} \Delta_{\mathbf{x}} V - \kappa_V V, & & & \partial_t v &= D_v \Delta_{\mathbf{x}} v - \sigma_v v, & \mathbf{x} &\in \Omega \setminus \bigcup_{j=1}^m \Omega_j, \end{aligned}$$

where we have defined the dimensionless effective diffusivities D_u and D_v and degradation rates σ_u and σ_v by

$$D_u \equiv \frac{D_U}{L^2 \kappa_R}, \quad \sigma_u \equiv \frac{\kappa_U}{\kappa_R}, \quad D_v \equiv \frac{D_V}{L^2 \kappa_R}, \quad \sigma_v \equiv \frac{\kappa_V}{\kappa_R}.$$

Since we assume that the common radius, denoted by L_c , of the cells is much smaller than the domain length-scale L , we introduce $\varepsilon \ll 1$ by $\varepsilon = L_c/L \ll 1$.

Next, by non-dimensionalizing the Robin boundary conditions in (2.2), we obtain

$$\begin{aligned} \frac{D_U}{L} \frac{\mu_c}{L^2} \partial_{n_{\mathbf{x}}} u &= \beta_{U,1} \frac{\mu_c}{L^2} u - \beta_{U,2} \mu_c \mu_j, & \Leftrightarrow & & \varepsilon D_u \partial_{n_{\mathbf{x}}} u &= d_1^u u - d_2^u \mu_j, & \mathbf{x} &\in \partial \Omega_j, \\ \frac{D_V}{L} \frac{\mu_c}{L^2} \partial_{n_{\mathbf{x}}} v &= \beta_{V,1} \frac{\mu_c}{L^2} v - \beta_{V,2} \mu_c \eta_j, & & & \varepsilon D_v \partial_{n_{\mathbf{x}}} v &= d_1^v v - d_2^v \eta_j, & \mathbf{x} &\in \partial \Omega_j, \end{aligned}$$

where we have defined d_1^u , d_2^u , d_1^v , and d_2^v by

$$d_1^u \equiv \frac{\beta_{U,1}}{\kappa_R L} \varepsilon, \quad d_2^u \equiv \frac{\beta_{U,2} L}{\kappa_R} \varepsilon, \quad d_1^v \equiv \frac{\beta_{V,1}}{\kappa_R L} \varepsilon, \quad d_2^v \equiv \frac{\beta_{V,2} L}{\kappa_R} \varepsilon.$$

Here, in order that there is an $\mathcal{O}(1)$ exchange across the cell membranes we have assumed that $\frac{\beta_{U,1}}{\kappa_R L}$, $\frac{\beta_{U,2} L}{\kappa_R}$, $\frac{\beta_{V,1}}{\kappa_R L}$ and $\frac{\beta_{V,2} L}{\kappa_R}$ are all $\mathcal{O}(\varepsilon^{-1})$.

Lastly, we non-dimensionalize the intracellular reaction kinetics in (2.2) by

$$\begin{aligned} \kappa_R \mu_c \frac{d}{dt} \mu_j &= \kappa_R \mu_c f(\mu_j, \eta_j) + \int_{\partial \Omega_j} \left(\beta_{U,1} \frac{\mu_c L}{L^2} u - \beta_{U,2} \mu_c L \mu_j \right) dS_{\mathbf{x}}, \\ \kappa_R \mu_c \frac{d}{dt} \eta_j &= \kappa_R \mu_c g(\mu_j, \eta_j) + \int_{\partial \Omega_j} \left(\beta_{V,1} \frac{\mu_c L}{L^2} v - \beta_{V,2} \mu_c L \eta_j \right) dS_{\mathbf{x}}, \end{aligned}$$

which yields the dimensionless intracellular reactions

$$\frac{d\mu_j}{dt} = f(\mu_j, \eta_j) + \frac{1}{\varepsilon} \int_{\partial \Omega_j} (d_1^u u - d_2^u \mu_j) dS_{\mathbf{x}}, \quad \frac{d\eta_j}{dt} = g(\mu_j, \eta_j) + \frac{1}{\varepsilon} \int_{\partial \Omega_j} (d_1^v v - d_2^v \eta_j) dS_{\mathbf{x}},$$

for each $j \in \{1, \dots, m\}$. This completes the derivation of (2.3).

B Reduced-wave Green's function for the unit disk

When Ω is the unit disk, the reduced-wave Green's function $G_{\omega}(\mathbf{x}; \xi)$ and its regular part, satisfying (2.9) can be determined analytically using separation of variables as (see equations (6.10) and (6.11) of [20])

$$G_{\omega}(\mathbf{x}; \xi) = \frac{1}{2\pi} K_0(\omega |\mathbf{x} - \xi|) - \frac{1}{2\pi} \sum_{n=0}^{\infty} \beta_n \cos(n(\psi - \psi_0)) \frac{K'_n(\omega)}{I'_n(\omega)} I_n(\omega |\mathbf{x}|) I_n(\omega |\xi|), \quad (\text{B.1a})$$

$$R_{\omega}(\xi) = \frac{1}{2\pi} (\log 2 - \gamma_e - \log \omega) - \frac{1}{2\pi} \sum_{n=0}^{\infty} \beta_n \frac{K'_n(\omega)}{I'_n(\omega)} [I_n(\omega |\xi|)]^2, \quad (\text{B.1b})$$

where $\gamma_e \approx 0.5772$ is Euler's constant, and $I_n(z)$ and $K_n(z)$ are the modified Bessel functions of the first and second kind of order n , respectively. In (B.1), $\beta_0 \equiv 1$, $\beta_n \equiv 2$ for $n \geq 1$, while $\mathbf{x} \equiv |\mathbf{x}|(\cos \psi, \sin \psi)^T$, and $\xi \equiv |\xi|(\cos \psi_0, \sin \psi_0)^T$.

For a ring pattern where the cell centers \mathbf{x}_k for $k \in \{1, \dots, m\}$, are equidistantly spaced on a ring of radius r concentric within the unit disk, as in (4.1), all the Green's matrices used in the steady-state and linear stability analysis are circulant and symmetric matrices. As a result, each such matrix spectrum is available analytically.

Following Appendix A of [50], for an $m \times m$ circulant matrix \mathcal{A} , with possibly complex-valued matrix entries, its complex-valued eigenvectors $\tilde{\mathbf{v}}_j$ and eigenvalues α_j are $\alpha_j = \sum_{k=1}^m \mathcal{A}_{1k} \omega_j^{k-1}$ and $\tilde{\mathbf{v}}_j = (1, Z_j, \dots, Z_j^{m-1})^T$, for $j \in \{1, \dots, m\}$. Here $Z_j \equiv \exp\left(\frac{2\pi i(j-1)}{m}\right)$ and \mathcal{A}_{1k} , for $k \in \{1, \dots, m\}$, are the elements of the first row of \mathcal{A} . Since \mathcal{A} is also a symmetric matrix, we have $\mathcal{A}_{1,j} = \mathcal{A}_{1,m+2-j}$, for $j \in \{2, \dots, \lceil m/2 \rceil\}$, where the ceiling function $\lceil x \rceil$ is defined as the smallest integer not less than x . Therefore, $\alpha_j = \alpha_{m+2-j}$, for $j \in \{2, \dots, \lceil m/2 \rceil\}$, so that there are $m-1$ eigenvalues with a multiplicity of two when m is odd, and $m-2$ such eigenvalues when m is even. As a result, we conclude that $\frac{1}{2}[\tilde{\mathbf{v}}_j + \tilde{\mathbf{v}}_{m+2-j}]$ and $\frac{1}{2i}[\tilde{\mathbf{v}}_j - \tilde{\mathbf{v}}_{m+2-j}]$ are two independent real-valued eigenvectors of \mathcal{A} , corresponding to the eigenvalues of multiplicity two. In summary, the matrix spectrum of a circulant and symmetric matrix \mathcal{A} , where the eigenvectors have been normalized by $\mathbf{v}_j^T \mathbf{v}_j = 1$, is

$$\alpha_j = \sum_{k=1}^m \mathcal{A}_{1k} \cos(\theta_j(k-1)), \quad j \in \{1, \dots, m\}; \quad \theta_j \equiv \frac{2\pi(j-1)}{m}; \quad \mathbf{v}_1 = \frac{1}{\sqrt{m}} \mathbf{e}, \quad (\text{B.2a})$$

$$\mathbf{v}_j = \sqrt{\frac{2}{m}} (1, \cos(\theta_j), \dots, \cos(\theta_j(m-1)))^T, \quad \mathbf{v}_{m+2-j} = \sqrt{\frac{2}{m}} (0, \sin(\theta_j), \dots, \sin(\theta_j(m-1)))^T \quad (\text{B.2b})$$

for $j \in \{2, \dots, \lceil m/2 \rceil\}$, where $\theta_j \equiv 2\pi(j-1)/m$. When m is even, there is an additional normalized eigenvector of multiplicity one given by $\mathbf{v}_{m/2+1} = m^{-1/2}(1, -1, 1, \dots, -1)^T$.