



*Research article***Kinematic phase-wave propagation with weak diffusion sensitivity under an imposed phase gradient in a bounded IP_3 -mediated calcium model****Minsoo Kim***

Major of Data Science, Korea Maritime & Ocean University, Busan 49112, Republic of Korea

* **Correspondence:** Email: hikims@kmou.ac.kr.

Abstract: We study a one-dimensional IP_3 -mediated calcium reaction–diffusion model in a bounded domain, separating localized no-flux simulations from an imposed periodic phase-gradient diagnostic used to measure the phase-wave speed v_ϕ . We establish global well-posedness, positivity, invariant bounds, and homogeneous-state properties. Under an explicit smooth-branch assumption, a small-wavenumber phase-wave calculation yields $v_\phi(k) = \omega_0/k + \omega_2 k + O(k^3)$ with $\omega_2 = \delta_C D_{\text{eff},C} + \delta_P D_{\text{eff},P}$, so diffusion enters through a finite- k correction along a coherent phase-wave branch. Extended simulations use pre-specified Fourier-mode coherence and phase-linearity screening. In the calcium-diffusion sweep, coherent stationary $m = 1$ fits persist through $\delta_C = 0.05$, while no speed is assigned for $\delta_C \geq 0.1$ because the prescribed mode loses coherence. In the IP_3 -diffusion sweep, all runs over $\delta_P \in [0.005, 1.0]$ remain coherent with no systematic speed dependence resolved. For the accepted coherent states, reaction-parameter tests show that v_ϕ tracks the kinematic reference $v_{\text{kin}} = L_\phi/T_{\text{osc}}$. The reported propagation is therefore phase transport at a prescribed wavenumber rather than a Fisher-KPP-type invasion speed. These conclusions are specific to the present model, tested parameter ranges, and imposed phase-gradient protocol.

Keywords: reaction–diffusion system; calcium signaling; IP_3 dynamics; finite-domain propagation; phase waves; receptor dynamics; diffusion effects

Mathematics Subject Classification: 35K57, 92C40

1. Introduction

Intracellular calcium signaling plays a fundamental role in a wide range of cellular processes, including gene expression, muscle contraction, and signal transduction, as established by classical studies on calcium signaling [1] and comprehensive modern reviews summarizing its diverse biological roles [2]. Among various mechanisms, calcium dynamics mediated by inositol 1,4,5-trisphosphate (IP_3) exhibit rich spatiotemporal behaviors such as oscillations and wave propagation, as highlighted in

studies on elementary and global calcium signaling dynamics [3] and subsequent reviews emphasizing the complexity of calcium oscillations and wave propagation [4]. These phenomena arise from the interplay between calcium release from intracellular stores, diffusion in the cytosol, receptor-mediated feedback, and active reuptake processes.

Mathematical modeling provides a quantitative framework for connecting calcium-signaling mechanisms with reaction–diffusion wave theory. Detailed models of IP_3 receptor dynamics and calcium oscillations [5–7], together with broader calcium-signaling reviews [8, 9], have clarified how receptor feedback, calcium release, and calcium removal generate oscillatory intracellular dynamics. Reaction–diffusion models, in turn, have long been used to describe spatial propagation in biological media [10, 11]. A classical reference point is the Fisher–Kolmogorov–Petrovsky–Piskunov (Fisher–KPP) equation

$$u_t = Du_{xx} + ru(1 - u), \quad r > 0,$$

which, on the real line, admits invasion fronts with minimal speed $v_* = 2\sqrt{Dr}$. Hence $v_* \propto \sqrt{D}$ provides the canonical diffusion-controlled scaling for this monostable invasion problem [12–15].

IP_3 -mediated calcium waves differ from this classical setting in two important ways. First, the relevant local dynamics are not simply monostable; receptor-mediated feedback and SERCA uptake can place the homogeneous kinetics in an oscillatory regime. In oscillatory reaction–diffusion media, propagation can be more naturally interpreted in terms of phase or kinematic waves, namely spatial sweeps of oscillation phase organized by diffusive coupling, rather than as Fisher–KPP invasion fronts [16]. This distinction is also consistent with calcium-wave classifications distinguishing trigger waves from kinematic or phase-wave-like mechanisms [17, 18]. For a coherent imposed phase pattern, the leading phase-wave speed may instead be set by the local oscillation period together with the prescribed wavenumber. Second, intracellular domains are bounded. In a spatially unbounded setting, a front speed may be selected through a traveling-wave or invasion mechanism; in a finite cell-like interval, the measured propagation depends on the stimulus location, boundary interaction, and diagnostic protocol.

Fisher–KPP theory provides a classical reference for diffusion-controlled invasion, whereas the present study concerns phase transport in an oscillatory medium under an imposed wavenumber. The two quantities arise from different domains, initial data, and selection mechanisms. A separate Fisher–KPP front-tracking control is reported in the Supplementary Material to verify that the numerical implementation recovers the expected $\sqrt{D}$ scaling for a classical invasion problem.

The quantitative question addressed here is what sets the phase-wave speed in a bounded, oscillatory IP_3 -mediated calcium model and how strongly that speed depends on the diffusion coefficients within coherent states generated by the imposed phase-gradient protocol.

To address this issue, we propose and analyze a one-dimensional reaction–diffusion model for IP_3 -mediated intracellular calcium dynamics. The model incorporates calcium diffusion, IP_3 dynamics, receptor-mediated release, and SERCA pump uptake, allowing us to examine the interplay between transport and reaction mechanisms. The primary propagation quantity reported in the numerical study is the phase-wave speed v_ϕ . Localized threshold-front measurements are retained only as auxiliary diagnostics for stimulus-driven simulations and are reported separately from v_ϕ .

The main contributions are as follows. First, we formulate the IP_3 -mediated calcium model on a specified bounded interval with admissible initial data and boundary conditions. Second, we establish global well-posedness, positivity, uniform boundedness, and invariance of the biologically relevant

region in $C(\overline{\Omega})^3$. Third, we characterize homogeneous stationary states, prove linear stability of the unstimulated rest state, and identify a candidate linear oscillatory-instability marker along a positive-equilibrium branch. Fourth, under explicit limit-cycle and smooth-branch assumptions, we derive a small-wavenumber phase-wave expansion and its leading kinematic consequence: $v_\phi - v_{\text{kin}} = O(k)$ along a coherent branch. Finally, the numerical study applies pre-specified coherence screening to diffusion sweeps, domain-size tests, crest-number tests, and direct comparisons between reaction-controlled oscillation periods and measured phase-wave speeds. The calcium sweep separates a coherent low-to-moderate diffusion branch from larger values at which the imposed $m = 1$ mode loses stationary coherence, whereas the IP_3 sweep remains coherent over $\delta_P \in [0.005, 1.0]$ with no systematic speed dependence resolved. Numerical refinement checks and the Fisher–KPP front-tracking control are reported in the Supplementary Material.

2. Model formulation

In this section, we present a reaction–diffusion model for IP_3 -mediated intracellular calcium dynamics. The model is constructed to capture the interplay between diffusion and nonlinear reaction mechanisms, with the aim of clarifying their respective roles in wave propagation.

2.1. Biological background

Intracellular calcium signaling mediated by IP_3 plays a key role in various cellular processes. Figure 1 illustrates the main biochemical mechanisms underlying this pathway. The underlying biological mechanisms have been extensively investigated in the literature, including early studies on IP_3 -mediated calcium signaling [1], comprehensive reviews of calcium signaling pathways and their cellular functions [2], experimental studies on calcium wave propagation [17], analyses of intracellular calcium and IP_3 diffusion [19], and investigations of the hierarchical organization of calcium signals from local events to global waves [20].

Upon external stimulation, phospholipase C (PLC) is activated at the cell membrane, leading to the hydrolysis of phosphatidylinositol 4,5-bisphosphate (PIP_2). This reaction generates inositol 1,4,5-trisphosphate (IP_3), which diffuses into the cytosol. The produced IP_3 binds to IP_3 -sensitive receptors located on the endoplasmic reticulum (ER) membrane, triggering the release of Ca^{2+} from the ER into the cytosol. The released calcium further participates in intracellular signaling through feedback mechanisms. At the same time, calcium is actively transported back into the ER via the sarco/endoplasmic reticulum Ca^{2+} -ATPase (SERCA) pump, maintaining intracellular calcium homeostasis.

This interplay between calcium release, diffusion, feedback regulation, and reuptake leads to complex spatiotemporal dynamics such as calcium oscillations and wave propagation. A central question is how nonlinear reaction kinetics and diffusion jointly shape phase transport and coherence under a specified bounded-domain protocol. To address this question, we construct a reaction–diffusion model incorporating these biological processes.

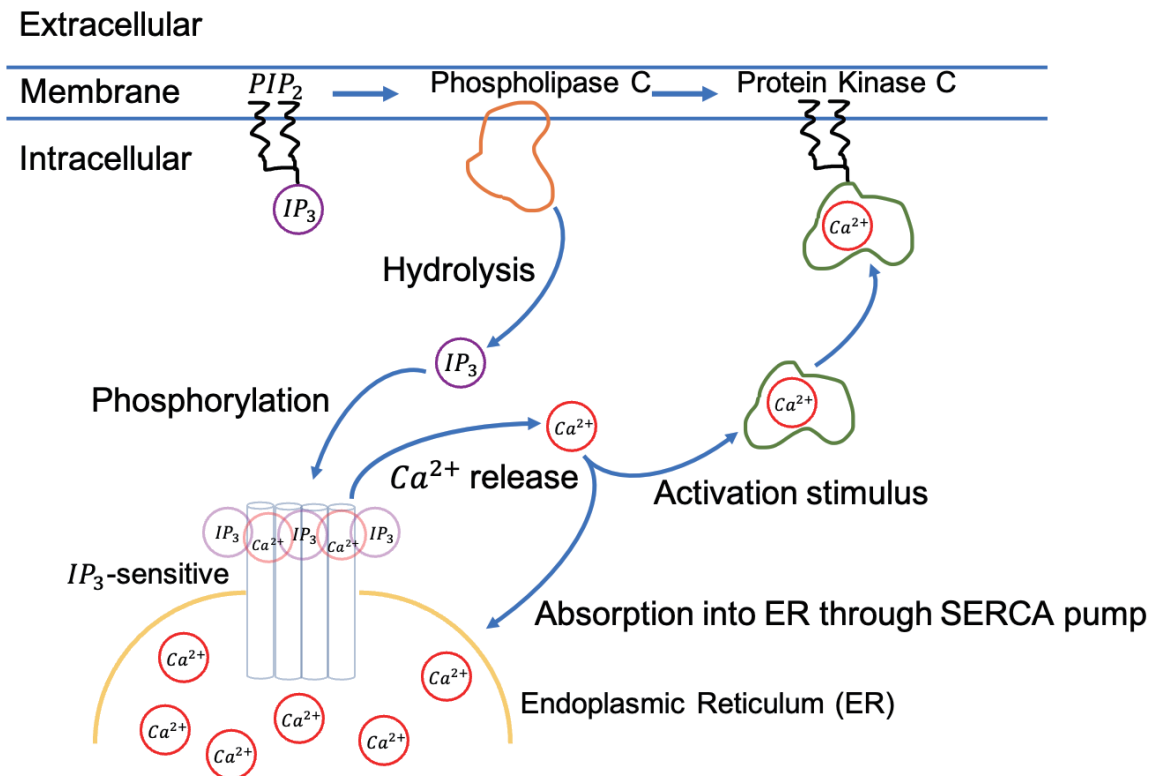


Figure 1. Schematic representation of the IP₃-mediated intracellular calcium signaling pathway. Upon external stimulation, phospholipase C (PLC) is activated at the cell membrane, leading to the hydrolysis of phosphatidylinositol 4,5-bisphosphate (PIP₂) and the production of inositol 1,4,5-trisphosphate (IP₃). The generated IP₃ diffuses into the cytosol and binds to IP₃-sensitive receptors located on the endoplasmic reticulum (ER), triggering the release of Ca²⁺ into the cytosol. The released calcium participates in intracellular signaling and may enhance further IP₃ production through feedback mechanisms. At the same time, calcium is transported back into the ER via the SERCA pump, maintaining intracellular calcium homeostasis. This interplay between diffusion, receptor-mediated release, feedback regulation, and calcium reuptake forms the basis of the reaction–diffusion model considered in this study.

2.2. Reaction–diffusion model

We first state the dimensional formulation. Dimensional variables and kinetic parameters are denoted by hats, while D_C and D_P denote the dimensional diffusion coefficients. On the physical interval $\Omega_L = (0, L)$, the dependent variables are the cytosolic calcium concentration $\widehat{C}(\widehat{x}, \widehat{t})$, the intracellular IP₃ concentration $\widehat{P}(\widehat{x}, \widehat{t})$, and the fraction of available receptors $\widehat{H}(\widehat{x}, \widehat{t})$. The variables $\widehat{C}$ and $\widehat{P}$ diffuse in the cytosolic direction, whereas $\widehat{H}$ is a local receptor-availability variable and has no diffusion term.

The dimensional equations are

$$\frac{\partial \widehat{C}}{\partial \widehat{t}} = D_C \frac{\partial^2 \widehat{C}}{\partial \widehat{x}^2} + \widehat{\alpha} \frac{\widehat{P}}{\widehat{\kappa}_P + \widehat{P}} \frac{\widehat{C}}{\widehat{\kappa}_A + \widehat{C}} \widehat{H} - \widehat{\beta} \frac{\widehat{C}^2}{\widehat{\kappa}_S^2 + \widehat{C}^2} - \widehat{\mu} \widehat{C}, \quad (2.1)$$

$$\frac{\partial \widehat{P}}{\partial t} = D_P \frac{\partial^2 \widehat{P}}{\partial \widehat{x}^2} + \widehat{\gamma} \frac{\widehat{S}(\widehat{x}, \widehat{t})}{\widehat{\kappa}_0 + \widehat{S}(\widehat{x}, \widehat{t})} + \widehat{\rho} \frac{\widehat{C}}{\widehat{\kappa}_C + \widehat{C}} - \widehat{\lambda} \widehat{P}, \quad (2.2)$$

$$\frac{\partial \widehat{H}}{\partial t} = \frac{1}{\widehat{\tau}} \left(\frac{\widehat{\kappa}_H^2}{\widehat{\kappa}_H^2 + \widehat{C}^2} - \widehat{H} \right). \quad (2.3)$$

They are supplemented with homogeneous Neumann boundary conditions

$$\widehat{C}_{\widehat{x}}(0, \widehat{t}) = \widehat{C}_{\widehat{x}}(L, \widehat{t}) = 0, \quad \widehat{P}_{\widehat{x}}(0, \widehat{t}) = \widehat{P}_{\widehat{x}}(L, \widehat{t}) = 0, \quad \widehat{t} > 0, \quad (2.4)$$

and initial data

$$\widehat{C}(\widehat{x}, 0) = \widehat{C}_0(\widehat{x}), \quad \widehat{P}(\widehat{x}, 0) = \widehat{P}_0(\widehat{x}), \quad \widehat{H}(\widehat{x}, 0) = \widehat{H}_0(\widehat{x}), \quad \widehat{x} \in \Omega_L. \quad (2.5)$$

We assume $\widehat{C}_0, \widehat{P}_0, \widehat{H}_0 \in C(\overline{\Omega_L})$, with $\widehat{C}_0 \geq 0$, $\widehat{P}_0 \geq 0$, and $0 \leq \widehat{H}_0 \leq 1$ pointwise, and

$$\widehat{S} \in C(\overline{\Omega_L} \times [0, \infty)), \quad \widehat{S} \geq 0.$$

The localized Gaussian stimulus used in Section 4 satisfies these assumptions.

The parameters $\widehat{\alpha}$ and $\widehat{\beta}$ are maximal calcium-release and SERCA-uptake rates, $\widehat{\mu}$ is the linear calcium-loss rate, $\widehat{\gamma}$ and $\widehat{\rho}$ are stimulus-driven and calcium-dependent IP_3 production rates, $\widehat{\lambda}$ is the IP_3 degradation rate, and $\widehat{\tau}$ is the receptor-response time. The constants $\widehat{\kappa}_P$, $\widehat{\kappa}_A$, $\widehat{\kappa}_S$, $\widehat{\kappa}_0$, $\widehat{\kappa}_C$, and $\widehat{\kappa}_H$ are the corresponding saturation or threshold scales.

After nondimensionalization, L is reserved for the physical cell-length scale, whereas the length of the periodic phase-gradient interval is denoted by L_ϕ . For an imposed winding number m , the phase wavelength, wavenumber, homogeneous period, and kinematic reference speed are

$$\ell_{\text{wave}} = \frac{L_\phi}{m}, \quad k = \frac{2\pi m}{L_\phi}, \quad T_{\text{osc}} = \frac{2\pi}{\omega_0}, \quad v_{\text{kin}} = \frac{\ell_{\text{wave}}}{T_{\text{osc}}} = \frac{\omega_0}{k}.$$

The symbol v_ϕ denotes the measured phase-wave speed. The auxiliary threshold-front diagnostic v_{th} used for a localized numerical refinement check is defined in Supplementary Section S4.

The external stimulus is spatially localized and temporally decaying. Mechanistic models of IP_3 receptor dynamics and calcium oscillations have been extensively developed [21], and broader frameworks for calcium signaling and oscillatory behavior are reviewed in [8, 9]. Stochastic and spatial aspects of calcium release have also been studied in models of clustered receptor activity [22] and calcium-domain formation [23]. In the present formulation, diffusion enters only through the transport operators for calcium and IP_3 , while release, uptake, degradation, stimulus response, and receptor availability are contained in the nonlinear reaction terms. This separation allows the diffusion-dependent phase-wave speed correction and the persistence of the imposed coherent mode to be examined independently.

2.3. Non-dimensionalization

Let $T_0 > 0$ be a reference time scale. We introduce

$$x = \frac{\widehat{x}}{L}, \quad t = \frac{\widehat{t}}{T_0}, \quad C = \frac{\widehat{C}}{\widehat{\kappa}_A}, \quad P = \frac{\widehat{P}}{\widehat{\kappa}_P}, \quad S = \frac{\widehat{S}}{\widehat{\kappa}_0}, \quad H = \widehat{H}.$$

The dimensionless groups are

$$\begin{aligned}\delta_C &= \frac{T_0 D_C}{L^2}, & \delta_P &= \frac{T_0 D_P}{L^2}, & \alpha &= \frac{T_0 \widehat{\alpha}}{\widehat{\kappa}_A}, & \beta &= \frac{T_0 \widehat{\beta}}{\widehat{\kappa}_A}, \\ \mu &= T_0 \widehat{\mu}, & \gamma &= \frac{T_0 \widehat{\gamma}}{\widehat{\kappa}_P}, & \rho &= \frac{T_0 \widehat{\rho}}{\widehat{\kappa}_P}, & \lambda &= T_0 \widehat{\lambda}, \\ \varepsilon_H &= \frac{\widehat{\tau}}{T_0}, & \kappa_S &= \frac{\widehat{\kappa}_S}{\widehat{\kappa}_A}, & \kappa_C &= \frac{\widehat{\kappa}_C}{\widehat{\kappa}_A}, & \kappa_H &= \frac{\widehat{\kappa}_H}{\widehat{\kappa}_A}.\end{aligned}$$

The scales $\widehat{\kappa}_P$, $\widehat{\kappa}_A$, and $\widehat{\kappa}_0$ are therefore absorbed into P , C , and S , respectively. The nondimensional domain is $\Omega = (0, 1)$, and hats are omitted below. The resulting system is

$$\frac{\partial C}{\partial t} = \delta_C \frac{\partial^2 C}{\partial x^2} + \alpha \frac{P}{1+P} \frac{C}{1+C} H - \beta \frac{C^2}{\kappa_S^2 + C^2} - \mu C, \quad (2.6)$$

$$\frac{\partial P}{\partial t} = \delta_P \frac{\partial^2 P}{\partial x^2} + \gamma \frac{S(x, t)}{1+S(x, t)} + \rho \frac{C}{\kappa_C + C} - \lambda P, \quad (2.7)$$

$$\frac{\partial H}{\partial t} = \frac{1}{\varepsilon_H} \left(\frac{\kappa_H^2}{\kappa_H^2 + C^2} - H \right). \quad (2.8)$$

The nondimensional boundary and initial conditions are

$$C_x(0, t) = C_x(1, t) = 0, \quad P_x(0, t) = P_x(1, t) = 0, \quad (2.9)$$

$$C(x, 0) = C_0(x), \quad P(x, 0) = P_0(x), \quad H(x, 0) = H_0(x), \quad (2.10)$$

where

$$C_0(x) = \frac{\widehat{C}_0(Lx)}{\widehat{\kappa}_A}, \quad P_0(x) = \frac{\widehat{P}_0(Lx)}{\widehat{\kappa}_P}, \quad H_0(x) = \widehat{H}_0(Lx).$$

The parameters in Table 1 are treated as dimensionless effective parameters defining a reproducible oscillatory regime. The analysis does not assume a unique inverse calibration to a particular cell type.

3. Mathematical analysis

This section establishes the basic analytical properties needed for the numerical phase-wave study. We first prove global well-posedness, positivity, invariant bounds, and preservation of the biologically relevant region. We then characterize homogeneous stationary states and identify a candidate linear oscillatory-instability marker along a positive-equilibrium branch. Finally, under explicit branch assumptions, we derive the small-wavenumber phase-wave expansion and state its leading kinematic consequence.

3.1. Functional setting and basic analytical properties

We begin by establishing basic qualitative properties of the system, including positivity, boundedness, and invariance of the biologically relevant region. The analysis is carried out on $\Omega = (0, 1)$. Let

$$X = C(\overline{\Omega})^3, \quad \|(C, P, H)\|_X = \max\{\|C\|_\infty, \|P\|_\infty, \|H\|_\infty\},$$

and define the biologically admissible set

$$\mathcal{B} = \{(C, P, H) \in X : C \geq 0, P \geq 0, 0 \leq H \leq 1 \text{ on } \overline{\Omega}\}.$$

Let A_N denote the Neumann Laplacian on $C(\overline{\Omega})$,

$$A_N u = u_{xx}, \quad D(A_N) = \{u \in C^2(\overline{\Omega}) : u_x(0) = u_x(1) = 0\}.$$

Define

$$\mathcal{A} = \text{diag}(\delta_C A_N, \delta_P A_N, 0), \quad D(\mathcal{A}) = D(A_N) \times D(A_N) \times C(\overline{\Omega}).$$

The zero operator on $C(\overline{\Omega})$ is bounded and generates the identity semigroup. Since A_N generates the positive analytic Neumann heat semigroup, the product operator $\mathcal{A}$ generates the positive analytic C_0 -semigroup

$$\mathcal{T}(t) = \text{diag}(e^{t\delta_C A_N}, e^{t\delta_P A_N}, I)$$

on X by the standard product-semigroup construction [24, 25]. Let $\mathcal{R}(t, U)$ denote the reaction vector in (2.6)–(2.8), where $U = (C, P, H)^\top$. Since the denominators are separated from zero on a fixed open neighborhood of $\mathcal{B}$, the associated Nemytskii map is continuously Fréchet differentiable there and is locally Lipschitz on bounded subsets, uniformly for t in bounded intervals. The following theorem uses this strongly continuous semigroup framework.

Theorem 1 (Global well-posedness and invariant bounds). *Assume*

$$\delta_C, \delta_P, \mu, \lambda, \kappa_S, \kappa_C, \kappa_H, \varepsilon_H > 0, \quad \alpha, \beta, \gamma, \rho \geq 0,$$

and let $U_0 = (C_0, P_0, H_0) \in \mathcal{B}$. Suppose also that

$$S \in C(\overline{\Omega} \times [0, \infty)), \quad S \geq 0.$$

Then the nondimensional system (2.6)–(2.8), together with (2.9)–(2.10), admits a unique global mild solution

$$U \in C([0, \infty); X)$$

satisfying the variation-of-constants formula

$$U(t) = \mathcal{T}(t)U_0 + \int_0^t \mathcal{T}(t-s)\mathcal{R}(s, U(s)) ds.$$

Moreover, $U(t) \in \mathcal{B}$ for every $t \geq 0$, and

$$0 \leq C(x, t) \leq M_C := \max \left\{ \|C_0\|_\infty, \frac{\alpha}{\mu} \right\},$$

$$0 \leq P(x, t) \leq M_P := \max \left\{ \|P_0\|_\infty, \frac{\gamma + \rho}{\lambda} \right\}, \quad 0 \leq H(x, t) \leq 1$$

for every $x \in \overline{\Omega}$ and $t \geq 0$. If, in addition, $U_0 \in D(\mathcal{A})$ and S is locally Hölder continuous in time with values in $C(\overline{\Omega})$, then the mild solution is classical.

Proof. Because $\mathcal{A}$ generates an analytic C_0 -semigroup on X and $\mathcal{R}$ is locally Lipschitz on bounded subsets of an open neighborhood of $\mathcal{B}$, standard semilinear evolution theory [24] yields a unique maximal mild solution

$$U \in C([0, T_{\max}); X).$$

It remains to establish invariance and bounds that exclude finite-time blow-up.

For each fixed x , the equation for H reduces to an ordinary differential equation. Since

$$0 < \frac{\kappa_H^2}{\kappa_H^2 + C^2} \leq 1,$$

it follows that the vector field points inward at $H = 0$ and $H = 1$. Therefore, the interval $[0, 1]$ is invariant under the flow, which implies

$$0 \leq H(x, t) \leq 1.$$

The reaction terms at $C = 0$ and $P = 0$ are nonnegative, and the diffusion operator with homogeneous Neumann boundary conditions preserves the maximum principle. Hence, the nonnegative cone is invariant.

Using the bounds

$$0 \leq \frac{S}{1+S} \leq 1, \quad 0 \leq \frac{C}{\kappa_C + C} \leq 1,$$

we obtain

$$\frac{\partial P}{\partial t} \leq \delta_P \frac{\partial^2 P}{\partial x^2} + \gamma + \rho - \lambda P.$$

Applying the comparison principle yields the stated bound for P . Similarly, since $0 \leq P/(1+P) \leq 1$, $0 \leq C/(1+C) \leq 1$, and $0 \leq H \leq 1$, the calcium equation satisfies

$$\frac{\partial C}{\partial t} \leq \delta_C \frac{\partial^2 C}{\partial x^2} + \alpha - \mu C.$$

The parabolic comparison principle then gives the stated bound for C . Consequently, the solution remains in the bounded subset $[0, M_C] \times [0, M_P] \times [0, 1]$ of the region on which $\mathcal{R}$ is locally Lipschitz. The continuation criterion for semilinear evolution equations therefore gives $T_{\max} = \infty$. $\square$

Remark 1. The continuity assumption on the initial data is used to place the problem in the standard strongly continuous semigroup framework on $C(\overline{\Omega})^3$. The estimates themselves are sup-norm estimates and are qualitative rather than sharp. For the parameter values of Table 1, the bounds α/μ and $(\gamma + \rho)/\lambda$ are much larger than the amplitudes observed numerically. The theorem is used only to guarantee global well-posedness and invariance of $\mathcal{B}$, not to provide quantitative amplitude estimates.

3.2. Homogeneous stationary states

We next discuss homogeneous stationary solutions. Because the external stimulus in the simulations is temporally decaying and spatially localized, the full forced system is generally nonautonomous and does not possess a time-independent equilibrium in the strict sense. It is nevertheless useful to characterize the homogeneous equilibria of the autonomous limiting system obtained after the stimulus has decayed, or more generally the system with a constant stimulus level $\bar{S} \geq 0$.

Let $C(x, t) \equiv C_*$, $P(x, t) \equiv P_*$, and $H(x, t) \equiv H_*$. Since the Neumann boundary conditions are automatically satisfied by spatially constant states, the stationary equations reduce to

$$0 = \alpha \frac{P_*}{1 + P_*} \frac{C_*}{1 + C_*} H_* - \beta \frac{C_*^2}{\kappa_S^2 + C_*^2} - \mu C_*, \quad (3.1)$$

$$0 = \gamma \frac{\bar{S}}{1 + \bar{S}} + \rho \frac{C_*}{\kappa_C + C_*} - \lambda P_*, \quad (3.2)$$

$$0 = \frac{\kappa_H^2}{\kappa_H^2 + C_*^2} - H_*. \quad (3.3)$$

Thus

$$H_*(C_*) = \frac{\kappa_H^2}{\kappa_H^2 + C_*^2}, \quad P_*(C_*; \bar{S}) = \frac{1}{\lambda} \left(\gamma \frac{\bar{S}}{1 + \bar{S}} + \rho \frac{C_*}{\kappa_C + C_*} \right).$$

Substituting these expressions into (3.1) yields a scalar algebraic equation for $C_* \geq 0$:

$$\alpha \frac{P_*(C_*; \bar{S})}{1 + P_*(C_*; \bar{S})} \frac{C_*}{1 + C_*} \frac{\kappa_H^2}{\kappa_H^2 + C_*^2} - \beta \frac{C_*^2}{\kappa_S^2 + C_*^2} - \mu C_* = 0.$$

In the unstimulated limiting case $\bar{S} = 0$, the state

$$(C_*, P_*, H_*) = (0, 0, 1)$$

is always a homogeneous equilibrium. Positive homogeneous equilibria, when present, correspond to positive roots of the above scalar equation. Their number and stability depend on the release, uptake, and receptor parameters.

It is important to distinguish the rest equilibrium from the positive-equilibrium branch used in the linear oscillatory-instability calculation below. In the unstimulated limiting case, the rest state $(0, 0, 1)$ is always linearly stable. Indeed, the Jacobian at this state is

$$J_{\text{rest}} = \begin{pmatrix} -\mu & 0 & 0 \\ \rho/\kappa_C & -\lambda & 0 \\ 0 & 0 & -\varepsilon_H^{-1} \end{pmatrix},$$

whose eigenvalues are

$$-\mu, \quad -\lambda, \quad -\varepsilon_H^{-1}.$$

Thus the stable rest state and the finite-amplitude oscillatory response are distinct dynamical objects. The cycles used in the phase-gradient simulations correspond to a finite-amplitude attractor, or to an oscillatory branch associated with a positive homogeneous equilibrium when such a branch is present.

This observation clarifies the baseline homogeneous states of the model without requiring additional numerical simulations.

3.3. Linear oscillatory-instability marker

The homogeneous equilibria identified above provide a convenient linear marker for the parameter study. For a fixed constant stimulus level $\bar{S}$, define

$$F(C, P, H) = \alpha \frac{P}{1 + P} \frac{C}{1 + C} H - \beta \frac{C^2}{\kappa_S^2 + C^2} - \mu C,$$

$$G(C, P; \bar{S}) = \gamma \frac{\bar{S}}{1 + \bar{S}} + \rho \frac{C}{\kappa_C + C} - \lambda P, \quad Q(C) = \frac{\kappa_H^2}{\kappa_H^2 + C^2}.$$

The homogeneous autonomous kinetics are

$$\dot{C} = F(C, P, H), \quad \dot{P} = G(C, P; \bar{S}), \quad \dot{H} = \varepsilon_H^{-1}(Q(C) - H).$$

At a positive homogeneous equilibrium (C_*, P_*, H_*) , the Jacobian is

$$J_* = \begin{pmatrix} F_C & F_P & F_H \\ G_C & -\lambda & 0 \\ \varepsilon_H^{-1} Q'(C_*) & 0 & -\varepsilon_H^{-1} \end{pmatrix}_{(C_*, P_*, H_*)},$$

where

$$\begin{aligned} F_C &= \alpha \frac{P_*}{1 + P_*} \frac{H_*}{(1 + C_*)^2} - \beta \frac{2C_* \kappa_S^2}{(\kappa_S^2 + C_*^2)^2} - \mu, \\ F_P &= \alpha \frac{C_*}{1 + C_*} \frac{H_*}{(1 + P_*)^2}, \quad F_H = \alpha \frac{P_*}{1 + P_*} \frac{C_*}{1 + C_*}, \\ G_C &= \rho \frac{\kappa_C}{(\kappa_C + C_*)^2}, \quad Q'(C_*) = -\frac{2\kappa_H^2 C_*}{(\kappa_H^2 + C_*^2)^2}. \end{aligned}$$

Write the characteristic polynomial as

$$\chi(r) = r^3 + a_1 r^2 + a_2 r + a_3,$$

where $a_1 = -\text{tr } J_*$, a_2 is the sum of the principal 2×2 minors, and $a_3 = -\det J_*$. The Routh–Hurwitz conditions are [26]

$$a_1 > 0, \quad a_2 > 0, \quad a_3 > 0, \quad a_1 a_2 > a_3.$$

At the equality $a_1 a_2 = a_3$ with $a_1, a_2, a_3 > 0$, the polynomial factors as

$$\chi(r) = (r + a_1)(r^2 + a_2),$$

so the linearized spectrum contains $-a_1$ and the purely imaginary pair $\pm i\sqrt{a_2}$. We call this equality, evaluated along the computed positive-equilibrium branch, the *linear oscillatory-instability marker*. For the baseline parameter set it occurs at $\beta_{\text{lin}}^* \approx 0.270$. The marker is used only to organize the parameter study; the finite-amplitude limit cycles used in Section 4 are computed directly.

3.4. Small-wavenumber phase-wave expansion

The phase-gradient diagnostic initializes the medium on a homogeneous limit cycle with an imposed wavenumber. The standard phase-reduction and adjoint phase-response framework [16, 27, 28] then yields an explicit small-wavenumber expansion for the frequency and phase-wave speed along any smooth coherent branch satisfying the assumptions below.

Write the autonomous homogeneous kinetics, after the stimulus has decayed and with constant level $\bar{S}$, as $\dot{\mathbf{u}} = \mathbf{N}(\mathbf{u})$, where $\mathbf{u} = (C, P, H)^\top$ and

$$\mathbf{N}(\mathbf{u}) = \left(F(C, P, H), G(C, P; \bar{S}), \varepsilon_H^{-1}(Q(C) - H) \right)^\top,$$

and collect the diffusion coefficients in $\mathbf{D} = \text{diag}(\delta_C, \delta_P, 0)$, so that the spatial model reads $\mathbf{u}_t = \mathbf{D} \mathbf{u}_{xx} + \mathbf{N}(\mathbf{u})$. We assume that the homogeneous kinetics possess an orbitally stable hyperbolic limit cycle $\mathbf{U}_0(\phi)$, 2π -periodic in the phase ϕ , with angular frequency $\omega_0 > 0$, so that $\omega_0 \mathbf{U}'_0(\phi) = \mathbf{N}(\mathbf{U}_0(\phi))$. This is the finite-amplitude oscillatory regime documented numerically in Section 4; the linear stability calculation of Section 3.3 supplies the positive-branch marker used to organize the parameter study.

Two boundary-value problems are used. The localized-stimulus problem is posed on $\Omega = (0, 1)$ with the homogeneous no-flux conditions (2.9); its auxiliary threshold-front diagnostic is described in Supplementary Section S4. The phase-gradient problem is posed on $(0, L_\phi)$ with periodic boundary conditions, which are compatible with the imposed datum $\mathbf{U}_0(\theta_0 + kx)$, $k = 2\pi m/L_\phi$, and an integer winding number m . The first problem describes a stimulus-driven transient in a closed interval, whereas the second probes phase transport at a prescribed wavenumber.

Proposition 1 (Phase-wave speed expansion along a smooth coherent branch). *Assume that the homogeneous kinetics possess the orbitally stable hyperbolic limit cycle $\mathbf{U}_0$ described above. Let $q = k^2$. Suppose that there exist $q_0 > 0$ and a phase-normalized C^2 family*

$$[0, q_0) \ni q \mapsto (\mathbf{U}(\cdot; q), \omega(q)) \in C^2_{\text{per}}([0, 2\pi]; \mathbb{R}^3) \times \mathbb{R}$$

satisfying

$$\omega(q) \mathbf{U}_\phi(\phi; q) = q \mathbf{D} \mathbf{U}_{\phi\phi}(\phi; q) + \mathbf{N}(\mathbf{U}(\phi; q)), \quad \mathbf{U}(\cdot; 0) = \mathbf{U}_0, \quad \omega(0) = \omega_0,$$

together with the phase condition

$$\int_0^{2\pi} (\mathbf{U}(\phi; q) - \mathbf{U}_0(\phi)) \cdot \mathbf{U}'_0(\phi) d\phi = 0.$$

Writing $\tilde{\omega}(k) := \omega(k^2)$, one has

$$\tilde{\omega}(k) = \omega_0 + \omega_2 k^2 + O(k^4), \quad \omega_2 = \delta_C D_{\text{eff},C} + \delta_P D_{\text{eff},P},$$

where

$$D_{\text{eff},j} = \langle \mathbf{Z}_j, \mathbf{U}''_{0,j} \rangle = -\langle \mathbf{Z}'_j, \mathbf{U}'_{0,j} \rangle, \quad j \in \{C, P\},$$

$\langle \mathbf{a}, \mathbf{b} \rangle = (2\pi)^{-1} \int_0^{2\pi} \mathbf{a}(\phi) \cdot \mathbf{b}(\phi) d\phi$, and $\mathbf{Z}(\phi)$ is the 2π -periodic adjoint neutral mode normalized by $\langle \mathbf{Z}, \mathbf{U}'_0 \rangle = 1$. Consequently, for $k > 0$,

$$v_\phi(k) = \frac{\tilde{\omega}(k)}{k} = \frac{\omega_0}{k} + (\delta_C D_{\text{eff},C} + \delta_P D_{\text{eff},P})k + O(k^3).$$

Proof. By the assumed C^2 dependence on q , write

$$\mathbf{U}(\phi; q) = \mathbf{U}_0(\phi) + q \mathbf{U}_2(\phi) + O(q^2), \quad \omega(q) = \omega_0 + q \omega_2 + O(q^2).$$

Substitution into $\omega \mathbf{U}_\phi = q \mathbf{D} \mathbf{U}_{\phi\phi} + \mathbf{N}(\mathbf{U})$ gives, at order q^0 , $\omega_0 \mathbf{U}'_0 = \mathbf{N}(\mathbf{U}_0)$ and, at order q ,

$$\mathbf{J}(\phi) := D_{\mathbf{u}} \mathbf{N}(\mathbf{U}_0(\phi)), \quad \mathcal{L} \mathbf{U}_2 := (\omega_0 \partial_\phi - \mathbf{J}(\phi)) \mathbf{U}_2 = \mathbf{D} \mathbf{U}''_0 - \omega_2 \mathbf{U}'_0.$$

Differentiating the limit-cycle identity gives $\mathcal{L}\mathbf{U}'_0 = 0$. By hyperbolicity, $\ker \mathcal{L} = \text{span}\{\mathbf{U}'_0\}$. The Fredholm solvability condition requires the right-hand side to be orthogonal to $\ker \mathcal{L}^* = \text{span}\{\mathbf{Z}\}$, where

$$\omega_0 \mathbf{Z}' + \mathbf{J}(\phi)^\top \mathbf{Z} = 0, \quad \langle \mathbf{Z}, \mathbf{U}'_0 \rangle = 1.$$

Taking the inner product with $\mathbf{Z}$ gives $\omega_2 = \langle \mathbf{Z}, \mathbf{D}\mathbf{U}''_0 \rangle$. Since $\mathbf{D} = \text{diag}(\delta_C, \delta_P, 0)$, only the C and P components contribute. Periodic integration by parts yields $D_{\text{eff},j} = -\langle \mathbf{Z}'_j, \mathbf{U}'_{0,j} \rangle$, and division by k gives the stated speed expansion. $\square$

Corollary 1 (Leading kinematic relation). *Under the assumptions of Proposition 1,*

$$v_\phi(k) - v_{\text{kin}} = k(\delta_C D_{\text{eff},C} + \delta_P D_{\text{eff},P}) + O(k^3), \quad v_{\text{kin}} = \frac{\omega_0}{k}.$$

Hence the leading phase-wave speed is set by the homogeneous oscillation frequency and the imposed wavenumber, while the diffusion-dependent correction is $O(k)$ along a coherent smooth branch.

Corollary 1 gives the principal analytical conclusion in affirmative form: the homogeneous frequency and imposed wavenumber set the leading phase-wave speed, while the adjoint mode $\mathbf{Z}$ and limit-cycle curvature $\mathbf{U}''_0$ determine the sign and magnitude of the finite- k diffusion correction. The diffusion sweeps in Section 4.3 quantify this correction for the states that satisfy the prescribed coherence criteria.

At a fixed wavenumber k , Corollary 1 also gives

$$\frac{v_\phi(k) - v_{\text{kin}}}{v_{\text{kin}}} = \frac{\omega_2 k^2}{\omega_0} + O(k^4). \quad (3.4)$$

Thus a diffusion sweep at fixed k provides a consistency test for the predicted linear dependence of the leading correction. Because the simulations use a single finite wavenumber and do not remove the $O(k^4)$ remainder, slopes inferred from the sweep are treated below as finite- k estimates rather than direct evaluations of the adjoint coefficients $D_{\text{eff},C}$ and $D_{\text{eff},P}$.

4. Numerical study of finite-domain phase-wave propagation

In this section, we present the numerical simulations used to quantify finite-domain phase transport. The term “wave” denotes a transient calcium elevation or a phase pattern measured under a specified bounded-domain protocol. The primary quantity in the periodic phase-gradient simulations is the phase-wave speed v_ϕ .

4.1. Numerical setup and phase-wave speed diagnostic

The simulations are performed on a one-dimensional spatial domain $(0, 1)$ with homogeneous Neumann (no-flux) boundary conditions for localized-stimulus calculations. The spatial domain is discretized using a uniform grid with $N_x = 400$ grid points, and the time integration is carried out with a time step $\Delta t = 0.001$. The total number of time steps is 6×10^6 , which ensures that the system reaches a long-time regime. For phase-wave diagnostics, we also use an extended finite interval $(0, L_\phi)$, typically $L_\phi = 40$, with periodic boundary conditions as explained in Section 3.4, so that several phase crests can be represented. The extended phase-domain simulations use $N_x^\phi = 400$ grid points unless

otherwise stated; for the largest crest number used in Figure 7, this still resolves the wavelength $L_\phi/6$ by approximately 67 grid intervals.

Diffusion terms are treated implicitly and reaction terms explicitly. The Neumann calculations lead to tridiagonal systems, while the periodic phase-gradient calculations lead to cyclic tridiagonal systems. In the latter case, the system matrix is written in the standard Sherman–Morrison form $B = T + \mathbf{u}\mathbf{v}^\top$, with T tridiagonal. After solving $T\mathbf{y} = \mathbf{b}$ and $T\mathbf{z} = \mathbf{u}$, the cyclic solution is

$$\mathbf{x} = \mathbf{y} - \mathbf{z} \frac{\mathbf{v}^\top \mathbf{y}}{1 + \mathbf{v}^\top \mathbf{z}}.$$

The Thomas/LU factors of T are precomputed because the matrix is fixed within each parameter run [29]. This implements $(I - \Delta t \delta_j D_{xx})u_j^{n+1} = \text{rhs}_j$ for $j \in \{C, P\}$. More specifically, if D_{xx} denotes the second-order central-difference approximation of the Laplacian, the diffusive variables are advanced by

$$\begin{aligned} \frac{C^{n+1} - C^n}{\Delta t} &= \delta_C D_{xx} C^{n+1} + F(C^n, P^n, H^n), \\ \frac{P^{n+1} - P^n}{\Delta t} &= \delta_P D_{xx} P^{n+1} + G(C^n, P^n, S^n), \end{aligned}$$

where F and G denote the reaction terms in the calcium and IP_3 equations. The receptor variable is updated explicitly by

$$H^{n+1} = H^n + \frac{\Delta t}{\varepsilon_H} \left(\frac{\kappa_H^2}{\kappa_H^2 + (C^n)^2} - H^n \right).$$

The homogeneous Neumann boundary condition is implemented by the standard reflected-node discretization, which enforces zero normal derivative at both endpoints. For the phase-gradient runs, D_{xx} is the corresponding periodic (circulant) stencil.

All numerical experiments and figure-generation scripts were written in Python 3 using NumPy, SciPy, Matplotlib, and Numba. The homogeneous autonomous kinetics were integrated with SciPy's DOP853 method using relative tolerance 10^{-10} , absolute tolerance 10^{-12} , and maximum step 0.2; the last two well-resolved calcium maxima after the long transient define T_{osc} , and the resulting cycle is interpolated periodically to construct the phase-gradient initial condition. The PDE computations use deterministic time stepping and precomputed direct factors for the implicit diffusion solves; hardware affects runtime but not the reported nondimensional quantities. These implementation details are included to improve reproducibility.

The external stimulus is assumed to be spatially localized and temporally decaying, given by

$$S(x, t) = S_0 \exp\left(-\frac{(x - x_0)^2}{\sigma^2}\right) \exp\left(-\frac{t}{\tau_s}\right),$$

where S_0 is the stimulus amplitude, x_0 is the center of stimulation, σ controls the spatial spread, and τ_s represents the temporal decay scale.

The baseline parameter values used in the simulations are summarized in Table 1. Most parameters are fixed throughout the simulations, while δ_C , δ_P , β , ε_H , α , and ρ are varied to investigate their influence on calcium dynamics and wave propagation. The parameters in Table 1 are dimensionless effective parameters. They are used to define a baseline oscillatory regime and to test whether the

main conclusions persist over reaction and diffusion parameter ranges, rather than to claim a unique biological calibration.

Table 1. Dimensionless model parameters used in numerical simulations.

Parameter	Description	Value	Parameter	Description	Value
$ \Omega $	Nondimensional localized-domain length	1.0	δ_C	Calcium diffusion	0.02 [0.005, 0.5]
N_x	Grid points	400	δ_P	IP ₃ diffusion	0.02 [0.005, 1.0]
Δt	Time step	10^{-3}	α	Ca release rate	3.50 (base; var.)
T_{end}	Total time	$6 \times 10^6 \Delta t$	β	SERCA rate	0.26 [0.14, 0.30]
μ	Ca decay	0.001	γ	IP ₃ production	4.20
ρ	Ca $\rightarrow$ IP ₃ feedback	2.40 (base; var.)	λ	IP ₃ decay	0.001 (base; Supp. var.)
κ_P	IP ₃ saturation	1.00 (scaled)	κ_A	Ca activation	1.00 (scaled)
κ_S	SERCA saturation	0.20	κ_C	Ca feedback	0.08
κ_H	Receptor inhibition	0.15	κ_0	Stimulus saturation	1.00 (scaled)
ε_H	Receptor timescale	70 [20, 250]	S_0	Stimulus amplitude	3.00
x_0	Stimulus center	0.50	σ	Spatial spread	0.08
τ_s	Temporal decay	60.0	C_0	Initial Ca	0.10
P_0	Initial IP ₃	0.05	H_0	Initial receptor	1.00
L_ϕ	Phase-domain length	40 (base; var.)	N_x^ϕ	Phase-grid points	400

The first value is the baseline value unless a parameter is explicitly swept; brackets indicate the sweep range. The constants κ_P , κ_A , and κ_0 are scaled to unity in the nondimensional system.

Because the homogeneous kinetics are oscillatory, localized stimulation can rapidly synchronize the finite domain and need not produce a sharp invasion front. We therefore use the phase-wave speed v_ϕ as the primary propagation diagnostic. Let $(C_{\text{LC}}(\theta), P_{\text{LC}}(\theta), H_{\text{LC}}(\theta))$ denote one numerically computed period of the homogeneous limit cycle, parameterized by phase $\theta \in [0, 2\pi)$. For a domain of length L_ϕ , we initialize the spatially extended system on this limit cycle with an imposed phase gradient,

$$(C(x, 0), P(x, 0), H(x, 0)) = (C_{\text{LC}}(\theta_0 + kx), P_{\text{LC}}(\theta_0 + kx), H_{\text{LC}}(\theta_0 + kx)), \quad k = \frac{2\pi m}{L_\phi},$$

where m is the number of imposed crests. The dominant Fourier phase is then defined by

$$A_k(t) = \int_0^{L_\phi} C(x, t) e^{-ikx} dx, \quad \phi(t) = \text{unwrap arg } A_k(t).$$

The phase-domain runs are integrated to $T_{\text{end}} = 6000$, and the Fourier phase is saved at intervals of 0.1. To make transient removal and speed assignment reproducible, three adjacent late-time windows are fixed in advance: [3000, 4000], [4000, 5000], and [5000, 6000]. A least-squares fit $\phi(t) \approx \omega t + \phi_0$ is performed on each window, and the central window provides the reported speed magnitude

$$v_\phi = \frac{|\omega|}{|k|}.$$

A run is accepted as a stationary coherent phase-wave fit only when all three windows satisfy $R^2 \geq 0.999$, the relative spread of their three fitted speeds is at most 1%, and the dominant-mode amplitude remains coherent in the sense that $\min |A_k| / \text{median } |A_k| \geq 0.20$ over the union of the fitting windows. If any criterion fails, no value of v_ϕ is assigned to that parameter case. This pre-specified screening prevents phase slips, mode collapse, or a nonstationary phase drift from being misreported as a phase-wave speed. The protocol measures transport of oscillation phase rather than the minimal speed of a

sharp concentration front. Figures 4, 5, 6, 7, and 8 use this v_ϕ protocol. The mesh/time-step refinement checks and the separate Fisher–KPP front-tracking control are reported in Supplementary Sections S4 and S5, respectively. The finite value of v_ϕ as $\delta_C, \delta_P \rightarrow 0$ in the imposed phase-gradient diagnostic means that, once an oscillatory phase pattern is prescribed, the leading phase-wave speed is set by the local oscillation frequency and imposed wavenumber.

The localized no-flux calculations also use an auxiliary threshold-front diagnostic solely for an implementation/refinement check. Its definition, threshold dependence, and mesh results are given in Supplementary Section S4, separately from the phase-wave speed v_ϕ . The same section reports empirical mesh and time-step sensitivity checks for v_ϕ .

4.2. Homogeneous oscillatory kinetics and reaction-parameter effects

We first examine the spatially homogeneous kinetics supporting the phase-wave interpretation. Figure 2 summarizes the dependence of oscillation amplitude on the SERCA uptake rate β , the receptor timescale ε_H , and their combined parameter plane. For $\varepsilon_H = 70$, the finite-amplitude oscillatory response persists throughout the displayed β range and decreases rapidly near the positive-equilibrium linear marker $\beta_{\text{lin}}^* \approx 0.270$. The persistence of the nonlinear cycle across this marker shows that the linear stability condition and the finite-amplitude cycle amplitude describe distinct properties of the homogeneous kinetics. For fixed $\beta = 0.26$, the amplitude increases nearly monotonically with ε_H , showing that slower receptor dynamics promote calcium accumulation. The two-parameter map indicates that the oscillatory amplitude is organized primarily by receptor timescale and uptake strength.

The time series in Figure 3 further illustrates the role of SERCA uptake. Increasing β lowers the peak calcium level and shifts the oscillation waveform, while sustained oscillations persist over the displayed range. Mechanistically, stronger SERCA uptake removes cytosolic calcium more rapidly, whereas slower receptor recovery permits receptor-mediated release to remain active over a longer portion of the oscillation cycle.

To connect the homogeneous oscillation with spatial propagation, we next examine phase-wave diagnostics. Figure 4 shows a representative calcium limit cycle and a space–time calcium field with diagonal bands of nearly constant phase. This pattern supports the interpretation of the observed propagation as phase-wave-like activity within the finite-amplitude oscillatory regime sampled by the imposed phase-gradient protocol.

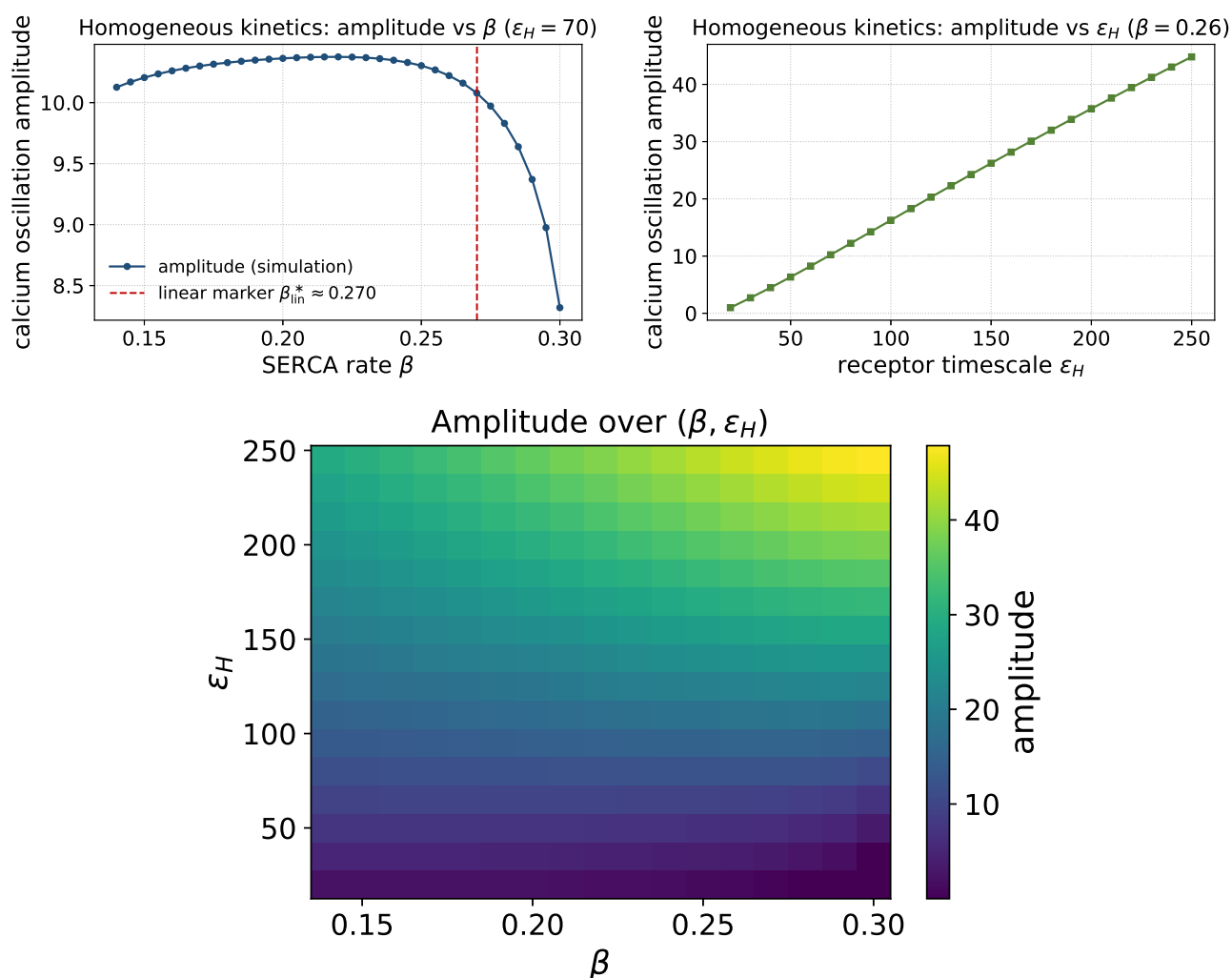


Figure 2. Homogeneous oscillatory kinetics. Top left: calcium oscillation amplitude as a function of the SERCA rate β at $\epsilon_H = 70$. The dashed vertical line marks the positive-equilibrium linear oscillatory-instability marker $\beta_{lin}^* \approx 0.270$; the simulated finite-amplitude branch persists across this marker. Top right: amplitude as a function of receptor timescale ϵ_H at $\beta = 0.26$. Bottom: amplitude over the (β, ϵ_H) parameter plane.

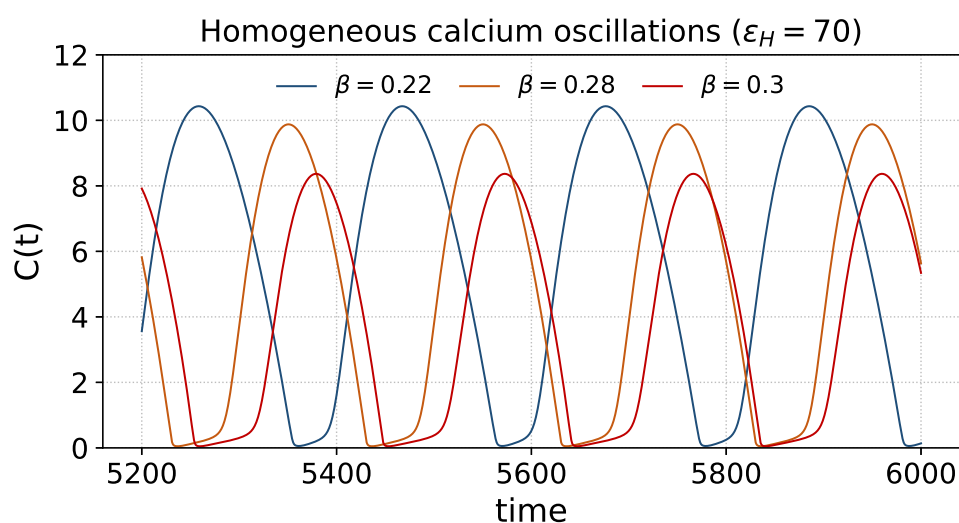


Figure 3. Representative homogeneous calcium oscillations for different SERCA rates β at $\varepsilon_H = 70$. The amplitude decreases as β increases, demonstrating the damping effect of enhanced calcium reuptake. The finite-amplitude oscillations persist across the displayed neighborhood of β_{lin}^* .

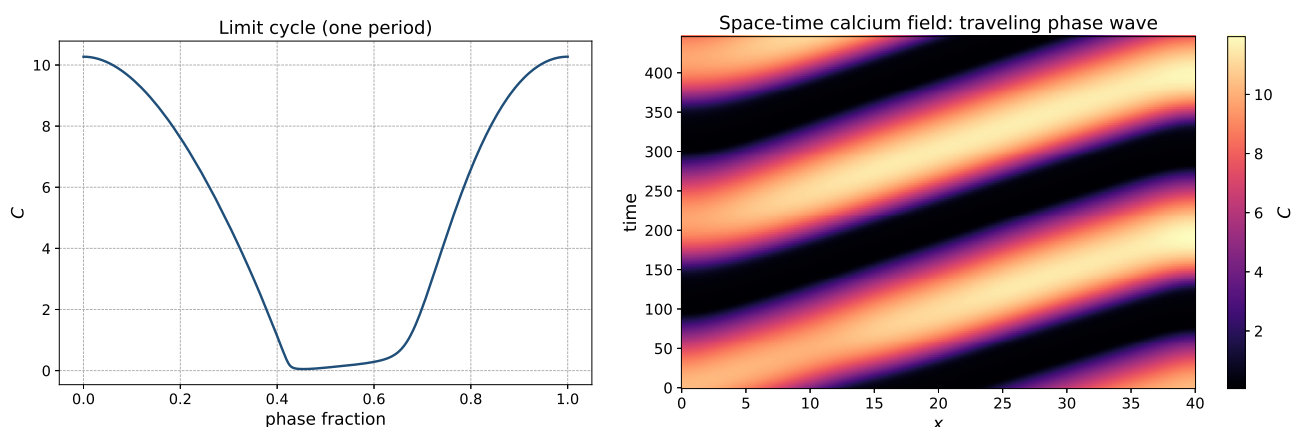


Figure 4. Phase-wave diagnostics. Left: one normalized period of the calcium limit cycle. Right: space-time calcium field showing diagonal bands of constant phase, characteristic of kinematic or phase-wave-like propagation within the sampled finite-amplitude oscillatory regime.

4.3. Diffusion sweeps under phase-coherence screening

We next examine extended diffusion sweeps under the pre-specified coherence and phase-linearity screening of Section 4.1. All runs in Figure 5 use $L_\phi = 40$ and one imposed crest, $m = 1$, so that $k_1 = 2\pi/40 \approx 0.157$ and $\omega_0/k_1^2 = 1.2591$ at the baseline parameter set. A phase-wave speed is reported only for runs that retain a coherent dominant Fourier mode and a stationary linear phase over all three late-time fitting windows.

In the calcium-diffusion sweep at fixed $\delta_P = 0.02$, the runs at $\delta_C = 0.005, 0.01, 0.02$, and 0.05 satisfy the screening criteria. For the three smallest accepted values,

$$\frac{v_{\text{kin}} - v_\phi}{v_{\text{kin}} \delta_C} = 0.397, \quad 0.400, \quad 0.408,$$

so the normalized deficit is proportional to δ_C to within approximately 3%. This is consistent with the leading linear dependence in (3.4). If the unresolved fixed- δ_P contribution and the $O(k^4)$ remainder are neglected, the corresponding finite- k slope gives an approximate value $D_{\text{eff},C} \approx -0.50$. We use this value only as a consistency estimate, not as a direct adjoint calculation. At $\delta_C = 0.05$, the ratio decreases to 0.373, indicating that the linear approximation weakens as the coherence boundary is approached. At $\delta_C = 0.1, 0.2, 0.3$, and 0.5 , the prescribed $m = 1$ pattern does not retain a stationary coherent phase fit, so no value of v_ϕ is assigned. Calcium diffusion therefore produces a measurable finite- k correction along the accepted branch and, at larger tested values, loss of the prescribed coherent mode.

In the IP₃-diffusion sweep at fixed $\delta_C = 0.02$, every run remains coherent over $\delta_P \in [0.005, 1.0]$. The total relative change in the fitted speed over this 200-fold interval is 1.9×10^{-6} , which is comparable to the numerical sensitivity indicated by the refinement checks in Supplementary Section S4. We therefore do not estimate $D_{\text{eff},P}$ from this sweep and retain the conclusion that no systematic δ_P dependence is resolved at the present numerical resolution. Supplementary Table S1 and Supplementary Figure S1 provide a mechanism check: the baseline limit cycle lies in a nearly saturated IP₃-release regime, while increasing λ moves the cycle into less-saturated regimes in which a larger δ_P -dependent finite- k correction becomes resolvable. A direct adjoint phase-response calculation is required to determine $D_{\text{eff},P}$ independently of the finite- k numerical uncertainty.

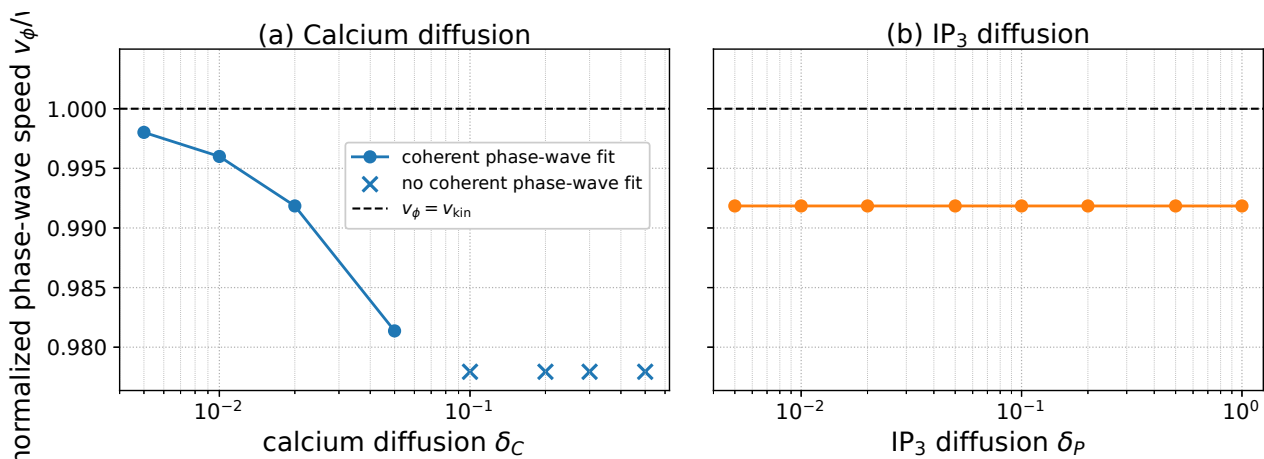


Figure 5. Extended diffusion sweeps under phase-coherence screening at $L_\phi = 40$ and $m = 1$. The vertical axis shows the measured phase-wave speed normalized by the corresponding kinematic reference $v_{\text{kin}} = L_\phi/T_{\text{osc}} = \omega_0/k_1$. (a) Calcium-diffusion sweep over $\delta_C \in [0.005, 0.5]$ at fixed $\delta_P = 0.02$. Filled circles denote runs satisfying all prescribed Fourier-mode coherence and phase-linearity criteria. For $\delta_C \leq 0.02$, the accepted normalized deficits are approximately proportional to δ_C , providing a finite- k consistency check of the leading correction. Crosses indicate parameter values for which no coherent stationary $m = 1$ phase-wave fit was obtained; their vertical positions are categorical and do not represent measured phase-wave speeds. (b) IP₃-diffusion sweep over $\delta_P \in [0.005, 1.0]$ at fixed $\delta_C = 0.02$. All tested runs remained coherent, and no systematic dependence of v_ϕ on δ_P was resolved within the numerical accuracy of the present discretization. The dashed horizontal line denotes $v_\phi = v_{\text{kin}}$. The coherent/non-coherent classification near the calcium-diffusion transition was unchanged after doubling the phase-domain resolution and, separately, halving the time step; the detailed refinement results are reported in Supplementary Table S2.

To assess numerical robustness near the calcium-diffusion coherence transition, we repeated the calculations at $\delta_C = 0.05, 0.10$, and 0.20 after doubling the phase-domain resolution from $N_x^\phi = 400$ to 800 and, separately, halving the time step from $\Delta t = 10^{-3}$ to 5×10^{-4} . The classification was unchanged: all three settings at $\delta_C = 0.05$ were coherent, whereas all settings at $\delta_C = 0.10$ and 0.20 were non-coherent under the prescribed criteria. For $\delta_C = 0.05$, the relative variation of v_ϕ across the three settings was 0.0041% . The tested transition interval is therefore $0.05 < \delta_C < 0.10$; Supplementary Table S2 reports the complete diagnostics.

A separate Fisher–KPP front-tracking control is reported in Supplementary Section S5. It recovers the expected $2\sqrt{Dr}$ scaling for the classical monostable invasion problem and documents the front-tracking implementation.

We next test domain-size dependence at fixed phase wavelength $\ell_{\text{wave}} = 20$. As L_ϕ and the number of imposed crests are varied, the measured values remain close to $v_{\text{kin}} = \ell_{\text{wave}}/T_{\text{osc}}$ (Figure 6), supporting a bulk phase-wave interpretation over the tested domain sizes.

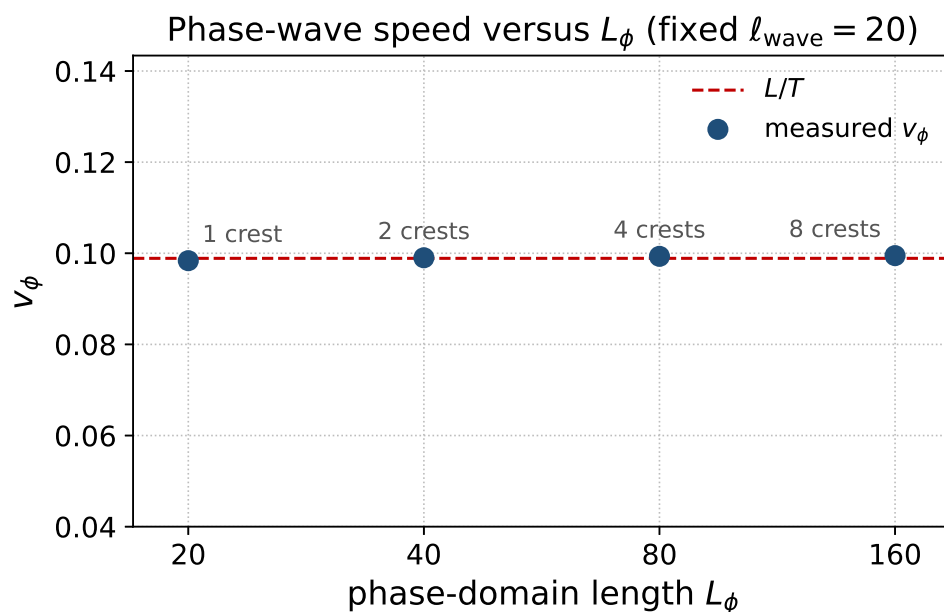


Figure 6. Domain-size dependence of the phase-wave speed. The phase wavelength $\ell_{\text{wave}} = 20$ is fixed while L_ϕ and the number of phase crests are varied. The dashed reference line denotes $v_{\text{kin}} = \ell_{\text{wave}}/T_{\text{osc}}$ (labelled L/T). The nearly constant measured values support a bulk phase-wave interpretation over the tested domain sizes.

4.4. Kinematic sensitivity and reaction-parameter control

The kinematic nature of the phase-wave speed is examined in Figure 7. For this diagnostic only, the two diffusion coefficients are set equal,

$$\delta_C = \delta_P =: D,$$

and the uncoupled case $D = 0$ is compared with $D = 0.01$. The left panel is the primary diagnostic: when the number of imposed crests m is varied at fixed L_ϕ , the measured speed decreases according to the leading relation $v_\phi \propto 1/k_m$, where $k_m = 2\pi m/L_\phi$. The right panel plots the normalized product

$$mv_\phi = \frac{L_\phi}{2\pi} k_m v_\phi.$$

Thus a horizontal curve in the right panel is equivalent to a constant $k_m v_\phi$. In particular, for the uncoupled $D = 0$ construction, $k_m v_\phi = \omega_0$, and the plotted constant reference is $mv_\phi = L_\phi/T_{\text{osc}}$.

The interpretation of the right panel requires care. For the uncoupled construction $D = 0$, the medium consists of independent oscillators, the relation $k_m v_\phi = \omega_0$ holds identically, and the normalized quantity mv_ϕ is constant. This panel therefore serves as an exact check of the leading kinematic relation and of the phase-extraction procedure, not as evidence about the model's diffusive behaviour.

For $D = 0.01$, the smallest crest numbers follow the small-wavenumber relation of Proposition 1. At larger m , the normalized product departs from the $D = 0$ reference by up to about 17%, indicating higher-order finite- k_m effects beyond the quadratic approximation $\tilde{\omega}(k_m) = \omega_0 + \omega_2 k_m^2 + O(k_m^4)$.

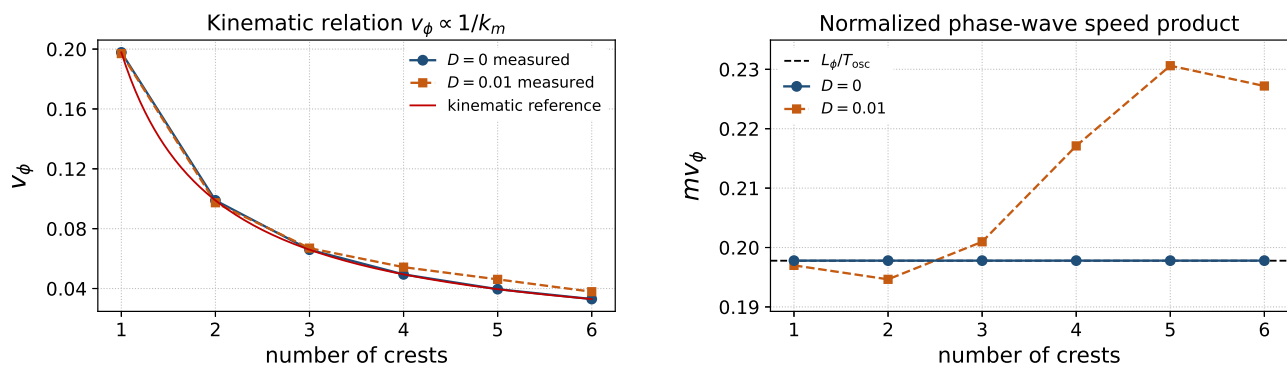


Figure 7. Kinematic sensitivity of the phase-wave speed. For this diagnostic, $\delta_C = \delta_P =: D$. Left: v_ϕ decreases with the number of imposed crests m , following the leading kinematic relation $v_\phi \propto 1/k_m$, where $k_m = 2\pi m/L_\phi$. Right: normalized phase-wave speed product $mv_\phi = (L_\phi/2\pi)k_mv_\phi$. The dashed reference line is L_ϕ/T_{osc} , equivalently the normalized form of $k_mv_\phi = \omega_0$. For $D = 0$, this product is constant up to numerical phase-extraction error. For $D = 0.01$, only the small- m portion lies within the small-wavenumber regime of Proposition 1; the large- m deviations are higher-order finite- k_m effects and are not interpreted here.

Finally, Figure 8 directly examines how representative reaction parameters alter the homogeneous oscillation period and the phase-wave speed. For each parameter set, the homogeneous finite-amplitude limit cycle was recomputed before the phase-gradient initial condition was constructed. Changes in the SERCA rate β and, more prominently, the receptor timescale ε_H substantially modify T_{osc} . The measured phase-wave speed follows the corresponding kinematic reference $v_{\text{kin}} = L_\phi/T_{\text{osc}}$, supporting the conclusion that the leading phase-wave speed is determined by the reaction-controlled oscillatory cycle rather than directly by the diffusion coefficients.

Across the coherent reaction-parameter cases in Figure 8, the observed residual $v_\phi - v_{\text{kin}}$ is not fixed in sign: it is negative in three displayed cases and positive for $\varepsilon_H = 150$. Because each case is sampled at one finite wavenumber, this observation is interpreted only as evidence that the finite- k residual depends on the reaction kinetics; it is not treated as a direct evaluation of ω_2 or of the adjoint coefficients.

A complementary robustness map over the calcium-release rate α and the calcium-to-IP₃ feedback rate ρ is provided in Supplementary Figure S2. The map documents the persistence and organization of the finite-amplitude homogeneous oscillatory regime over the tested (α, ρ) plane, while the period-speed comparison in Figure 8 provides the direct phase-wave speed evidence.

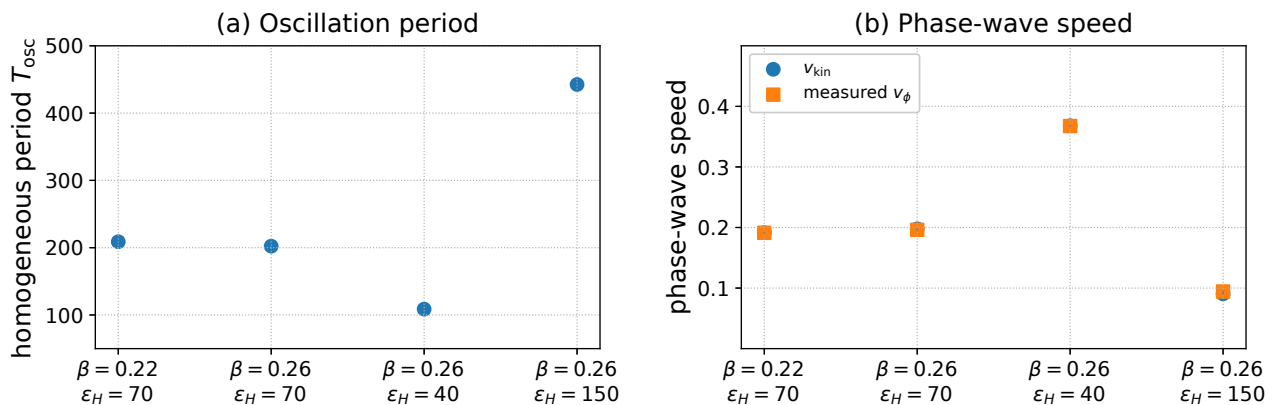


Figure 8. Reaction-parameter control of the homogeneous oscillation period and phase-wave speed. For each parameter set, the homogeneous finite-amplitude limit cycle was recomputed before constructing the imposed phase-gradient initial condition. Left: homogeneous oscillation period T_{osc} for representative values of the SERCA rate β and receptor timescale ϵ_H . Right: measured phase-wave speed v_ϕ compared with the corresponding kinematic reference $v_{\text{kin}} = L_\phi/T_{\text{osc}} = \omega_0/k_1$ at $L_\phi = 40$, $m = 1$, and $\delta_C = \delta_P = 0.02$. The measured speed tracks the reaction-set kinematic reference across the coherent cases, while the remaining discrepancy represents a finite- k diffusion correction. For $\beta = 0.30$ and $\epsilon_H = 70$, no coherent stationary $m = 1$ phase-wave fit satisfying the prescribed screening criteria was obtained, and therefore no value of v_ϕ is assigned for that case.

4.5. Reaction–diffusion interplay

Combining these simulations, we identify a division of roles that depends on whether a coherent phase-wave pattern is sustained. Along the coherent branch, the measured phase-wave speed remains close to the kinematic reference $v_{\text{kin}} = \omega_0/k$, with diffusion contributing a finite- k offset. Calcium diffusion also affects persistence of the imposed spatial phase pattern: at the larger tested δ_C values, the $m = 1$ Fourier mode fails the stationary coherence criteria and no speed is assigned. The approximate proportionality observed at the three smallest calcium-diffusion values provides a finite- k consistency check of the analytical expansion. By contrast, the IP_3 -diffusion variation remains comparable to the numerical refinement sensitivity, so no separate IP_3 coefficient is assigned. The reaction-parameter cases further show that the finite- k residual can depend on the underlying oscillatory kinetics without changing the leading kinematic relation. Supplementary Figure S1 supports near-saturation of the baseline IP_3 release gate as one contributor to the flat δ_P sweep, while Supplementary Figure S2 documents broad amplitude robustness over (α, ρ) .

5. Discussion

In this study, we investigated a reaction–diffusion model for IP_3 -mediated intracellular calcium dynamics, with emphasis on phase transport in a bounded domain. The mathematical formulation specifies the domain, boundary conditions, admissible initial data, and functional setting, and establishes well-posedness, positivity, uniform boundedness, homogeneous steady states, linear stability of the rest state, and a linear oscillatory-instability marker for positive homogeneous equilibria.

Proposition 1 and Corollary 1 organize the analytical interpretation: the leading phase-wave speed is $v_{\text{kin}} = \omega_0/k$, and diffusion enters through a finite- k correction along a coherent branch. The three smallest accepted calcium-diffusion values provide a quantitative finite- k consistency check: their normalized deficits are approximately proportional to δ_C , and the corresponding slope gives $D_{\text{eff},C} \approx -0.50$ only after the fixed- δ_P contribution and the $O(k^4)$ remainder are neglected. We therefore report this as a finite- k estimate rather than a direct adjoint coefficient. The IP_3 -diffusion variation remains comparable to the refinement sensitivity, so no value of $D_{\text{eff},P}$ is assigned. The reaction-parameter cases show that the observed finite- k residual can have either sign, which is consistent with its dependence on the limit cycle and adjoint mode rather than on a universal sign rule.

The supplementary Fisher–KPP calculation documents the front-tracking implementation in a classical monostable invasion problem. The present results instead concern phase transport in a bounded oscillatory medium under an imposed wavenumber, consistent with the phase- or kinematic-wave framework [16, 27] and with calcium-wave classifications distinguishing trigger and kinematic mechanisms [17, 18].

The numerical results show that the SERCA rate β and receptor timescale ε_H strongly shape the homogeneous oscillatory cycle. Increasing β reduces the calcium amplitude, while increasing ε_H changes both calcium accumulation and oscillation timing. The candidate marker β_{lin}^* organizes the positive-equilibrium linear stability calculation, and the directly computed finite-amplitude cycles persist across its displayed neighborhood. The period–speed comparison in Figure 8 supplies the relevant propagation evidence: after the limit cycle is recomputed in each coherent case, the measured phase-wave speed tracks L_ϕ/T_{osc} .

Mechanistically, the combined effect of β and ε_H can be understood as a release–reuptake balance. SERCA uptake removes cytosolic calcium and reduces the amplitude available for threshold crossing, whereas slower receptor recovery delays inactivation and allows receptor-mediated release to persist for a longer time. Consequently, oscillation amplitude, phase timing, and the phase-wave metric are organized by the competition between calcium release, receptor availability, and active reuptake.

The interpretation has three principal boundaries. First, the phase-gradient protocol imposes k , so it measures transport and coherence at a prescribed wavenumber rather than wavenumber selection by a localized stimulus. Second, the adjoint coefficients have not been computed directly. The slope inferred from the small- δ_C sweep is only a finite- k consistency estimate, and the δ_P effect remains below the present numerical resolution. Third, the calcium-diffusion coherence boundary is located numerically by the stated screening criteria. Extensions to selected wavenumbers, direct adjoint calculations, higher-dimensional or heterogeneous geometries, and stochastic receptor dynamics are natural next steps.

The conclusions are specific to the present one-dimensional model and to coherent states generated by the imposed periodic phase-gradient protocol; they should not be extrapolated to all IP_3 -mediated calcium fronts or to stimulus-selected invasion processes.

6. Conclusions

In this work, we proposed and analyzed a reaction–diffusion model for IP_3 -mediated intracellular calcium signaling, incorporating calcium diffusion, IP_3 dynamics, receptor-mediated release, and SERCA pump uptake.

Analytically, we established well-posedness, positivity, uniform boundedness, and invariance of the biologically relevant region; characterized homogeneous equilibria; identified a linear oscillatory-instability marker on a positive-equilibrium branch; and, under explicit branch assumptions, obtained $v_\phi(k) = \omega_0/k + \omega_2 k + O(k^3)$ together with $v_\phi - v_{\text{kin}} = O(k)$. Numerically, we applied reproducible late-time phase fits with explicit coherence screening, performed extended diffusion sweeps, checked domain-size and crest-number dependence, and compared reaction-controlled oscillation periods directly with measured phase-wave speeds. The Supplementary Material contains the gate-desaturation and reaction-parameter controls, numerical refinement checks, and the separate Fisher–KPP front-tracking control.

Within the accepted coherent states and tested parameter ranges, the phase-wave speed is kinematic at leading order: the homogeneous oscillation frequency ω_0 and imposed wavenumber k set $v_{\text{kin}} = \omega_0/k$, while diffusion contributes a finite- k correction. For the three smallest accepted calcium-diffusion values, the normalized deficit varies approximately linearly with δ_C , consistent with the leading finite- k correction. The IP_3 -diffusion sweep remains coherent, but its total variation is comparable to the refinement sensitivity, so no separate IP_3 coefficient is assigned. Across the coherent reaction-parameter cases, the observed finite- k residual can change sign, indicating kinetics dependence while preserving the leading relation $v_\phi \simeq \omega_0/k$ within the tested regime. These results describe coherent phase transport under the imposed periodic phase-gradient protocol, not a universal speed law for localized calcium fronts.

The proposed framework provides a basis for further investigation of intracellular signaling processes, in particular through direct computation of the adjoint phase-response curve, extension to higher-dimensional geometries, heterogeneous environments, and stochastic dynamics.

Supplementary material

The supplementary material contains the IP_3 release-gate saturation and desaturation control (Table S1 and Figure S1), the (α, ρ) amplitude-robustness map (Figure S2), the numerical robustness check near the calcium-diffusion coherence transition (Table S2), the auxiliary threshold-front diagnostic and mesh/time-step refinement checks (Figures S3–S4), and the Fisher–KPP front-tracking control (Figure S5).

Acknowledgments

This work was supported by the National Research Foundation of Korea (NRF) grant funded by the Korean government (MSIT) (RS-2026-25473191).

Conflict of interest

The author declares no conflict of interest.

Use of Generative-AI tools declaration

The author used ChatGPT (OpenAI, GPT-5.5) and Claude (Opus5) for language editing only. The tool was used to check English grammar, spelling, and punctuation, and to improve the readability of text written by the author. It was not used for analysis, for research design, or for language generation: the model formulation, the mathematical analysis, the numerical experiments, the figures and tables, and all interpretations and conclusions were produced by the author without AI assistance. No references were identified, selected, or generated by the tool. AI-assisted language editing was applied to the prose of the manuscript and of the supplementary material; no AI-generated content appears elsewhere in the article. The author takes full responsibility for the content, interpretation, and conclusions of this work.

References

1. M. J. Berridge, Inositol trisphosphate and calcium signalling, *Nature*, **361** (1993), 315–325. <https://doi.org/10.1038/361315a0>
2. D. E. Clapham, Calcium signaling, *Cell*, **131** (2007), 1047–1058. <https://doi.org/10.1016/j.cell.2007.11.028>
3. M. J. Berridge, Elementary and global aspects of calcium signalling, *J. Exp. Biol.*, **200** (1997), 315–319. <https://doi.org/10.1242/jeb.200.2.315>
4. M. J. Berridge, M. D. Bootman, H. L. Roderick, Calcium signalling: dynamics, homeostasis and remodelling, *Nat. Rev. Mol. Cell Bio.*, **4** (2003), 517–529. <https://doi.org/10.1038/nrm1155>
5. G. W. De Young, J. Keizer, A single-pool inositol 1,4,5-trisphosphate-receptor-based model for agonist-stimulated oscillations in Ca^{2+} concentration, *P. Natl. Acad. Sci. USA.*, **89** (1992), 9895–9899. <https://doi.org/10.1073/pnas.89.20.9895>
6. Y. X. Li, J. Rinzel, Equations for InsP_3 receptor-mediated Ca^{2+} oscillations derived from a detailed kinetic model: A Hodgkin–Huxley like formalism, *J. Theor. Biol.*, **166** (1994), 461–473. <https://doi.org/10.1006/jtbi.1994.1041>
7. J. Sneyd, M. Falcke, Models of the inositol trisphosphate receptor, *Prog. Biophys. Mol. Bio.*, **89** (2005), 207–245. <https://doi.org/10.1016/j.pbiomolbio.2004.11.001>
8. G. Dupont, L. Combettes, G. S. Bird, J. W. Putney, Calcium oscillations, *CSH Perspect. Biol.*, **3** (2011), a004226. <https://doi.org/10.1101/cshperspect.a004226>
9. G. Dupont, M. Falcke, V. Kirk, J. Sneyd, *Models of Calcium Signalling*, vol. 43 of Interdisciplinary Applied Mathematics, Springer, Cham, 2016. <https://doi.org/10.1007/978-3-319-29647-0>
10. J. Keener, J. Sneyd, *Mathematical Physiology II: Systems Physiology*, Springer, New York, 2009, <https://doi.org/10.1007/978-0-387-79388-7>
11. J. D. Murray, *Mathematical Biology II: Spatial Models and Biomedical Applications*, vol. 18 of Interdisciplinary Applied Mathematics, Springer, New York, 2003. <https://doi.org/10.1007/b98869>
12. R. A. Fisher, The wave of advance of advantageous genes, *Annals Eugenics*, **7** (1937), 355–369. <https://doi.org/10.1111/j.1469-1809.1937.tb02153.x>

13. A. Kolmogoroff, I. Petrovsky, N. Piscounoff, Study of the diffusion equation with growth of the quantity of matter and its application to a biology problem, in *Dynamics of Curved Fronts*. Elsevier, Amsterdam, 1988, 105–130. <https://doi.org/10.1016/B978-0-08-092523-3.50014-9>
14. D. G. Aronson, H. F. Weinberger, Nonlinear diffusion in population genetics, combustion, and nerve pulse propagation, in *Partial Differential Equations and Related Topics*. Springer, Berlin, 1975, 5–49. <https://doi.org/10.1007/BFb0070595>
15. W. van Saarloos, Front propagation into unstable states, *Phys. Rep.*, **386** (2003), 29–222. <https://doi.org/10.1016/j.physrep.2003.08.001>
16. N. Kopell, L. N. Howard, Plane wave solutions to reaction-diffusion equations, *Stud. Appl. Math.*, **52** (1973), 291–328. <https://doi.org/10.1002/sapm1973524291>
17. L. F. Jaffe, Classes and mechanisms of calcium waves, *Cell Calcium*, **14** (1993), 736–745. [https://doi.org/10.1016/0143-4160\(93\)90099-R](https://doi.org/10.1016/0143-4160(93)90099-R)
18. M. Falcke, Reading the patterns in living cells—the physics of Ca^{2+} signaling, *Adv. Phys.*, **53** (2004), 255–440. <https://doi.org/10.1080/00018730410001703159>
19. N. L. Allbritton, T. Meyer, L. Stryer, Range of messenger action of calcium ion and inositol 1,4,5-trisphosphate, *Science*, **258** (1992), 1812–1815. <https://doi.org/10.1126/science.1465619>
20. M. D. Bootman, M. J. Berridge, P. Lipp, Cooking with calcium: the recipes for composing global signals from elementary events, *Cell*, **91** (1997), 367–373. [https://doi.org/10.1016/S0092-8674\(00\)80420-1](https://doi.org/10.1016/S0092-8674(00)80420-1)
21. J. Sneyd, K. Tsaneva-Atanasova, D. I. Yule, J. Thompson, T. J. Shuttleworth, Control of calcium oscillations by membrane fluxes, *P. Natl. Acad. Sci. USA*, **101** (2004), 1392–1396. <https://doi.org/10.1073/pnas.0303472101>
22. J. W. Shuai, P. Jung, Stochastic properties of Ca^{2+} release of inositol 1,4,5-trisphosphate receptor clusters, *Biophys. J.*, **83** (2002), 87–97. [https://doi.org/10.1016/S0006-3495\(02\)75151-5](https://doi.org/10.1016/S0006-3495(02)75151-5)
23. S. Rüdiger, C. Nagaiah, G. Warnecke, J. Shuai, Calcium domains around single and clustered IP_3 receptors and their modulation by buffers, *Biophys. J.*, **99** (2010), 3–12. <https://doi.org/10.1016/j.bpj.2010.02.059>
24. D. Henry, *Geometric Theory of Semilinear Parabolic Equations*, vol. 840 of Lecture Notes in Mathematics, Springer-Verlag, Berlin, 1981. <https://doi.org/10.1007/BFb0089647>
25. K. J. Engel, R. Nagel, *One-Parameter Semigroups for Linear Evolution Equations*, vol. 194 of Graduate Texts in Mathematics, Springer, New York, 2000. <https://doi.org/10.1007/b97696>
26. Y. A. Kuznetsov, *Elements of Applied Bifurcation Theory*, vol. 112 of Applied Mathematical Sciences, 3rd edition, Springer, New York, 2004.
27. Y. Kuramoto, *Chemical Oscillations, Waves, and Turbulence*, vol. 19 of Springer Series in Synergetics, Springer-Verlag, Berlin, 1984. <https://doi.org/10.1007/978-3-642-69689-3>
28. G. B. Ermentrout, D. H. Terman, *Mathematical Foundations of Neuroscience*, vol. 35 of Interdisciplinary Applied Mathematics, Springer, New York, 2010. <https://doi.org/10.1007/978-0-387-87708-2>
29. G. H. Golub, C. F. Van Loan, *Matrix Computations*, 4th edition, Johns Hopkins University Press, Baltimore, 2013.

Supplementary material

S1. IP₃ release-gate saturation and desaturation control

The receptor-mediated calcium-release term contains the IP₃-dependent factor

$$g_P(P) = \frac{P}{1+P}, \quad g'_P(P) = \frac{1}{(1+P)^2}. \quad (\text{S1})$$

For the baseline parameter set, the homogeneous finite-amplitude limit cycle lies in a strongly saturated IP₃ regime. Table S1 reports the IP₃ range and the corresponding release-gate range for the baseline value $\lambda = 0.001$ and for two larger degradation rates used to reduce gate saturation. The limit cycle was recomputed at every value of λ by continuation from the preceding oscillatory state.

Table S1. IP₃ release-gate diagnostics along the homogeneous limit cycle.

λ	T_{osc}	$P_{\text{min}}-P_{\text{max}}$	$g_P(P)_{\text{min}}-g_P(P)_{\text{max}}$	$\max g'_P(P)$
0.001	202.25	2149.81–2178.55	0.999535–0.999541	2.162×10^{-7}
0.1	206.10	13.36–23.81	0.930361–0.959692	4.850×10^{-3}
0.3	210.40	3.26–7.94	0.765509–0.888114	5.499×10^{-2}

Figure S1 compares the loss of gate saturation with the IP₃-diffusion-dependent finite- k phase-wave speed correction. At the baseline value $\lambda = 0.001$, the release gate is nearly saturated and the correction is essentially flat over the tested δ_P range. When λ is increased, the release gate becomes substantially more sensitive to P , and a larger δ_P -dependent correction becomes resolvable. Because changing λ also changes the underlying homogeneous limit cycle, this control identifies gate saturation as a contributing mechanism; it does not prove that saturation is the sole origin of the baseline IP₃-diffusion insensitivity, nor does it replace a direct adjoint phase-response calculation.

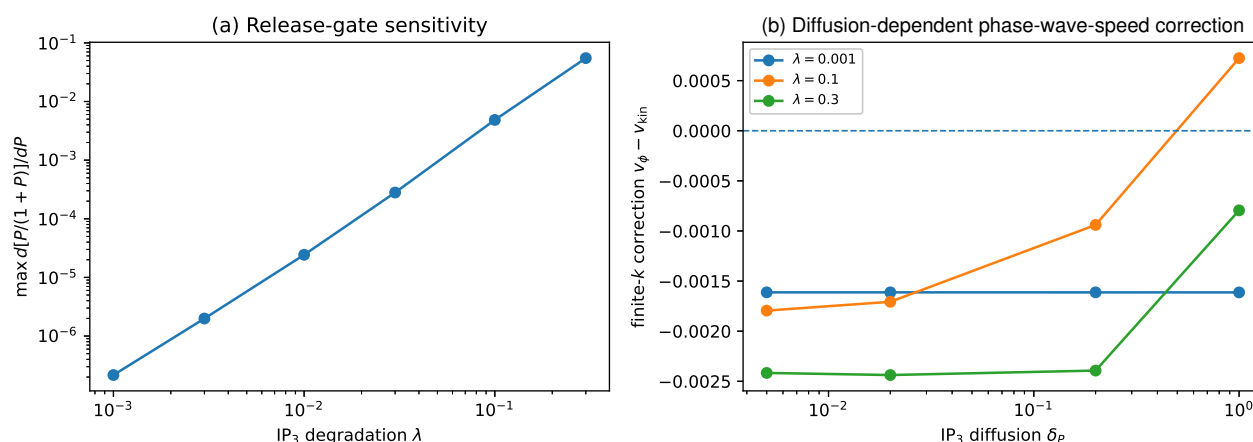
IP₃ gate desaturation and diffusion sensitivity

Figure S1. IP₃ release-gate desaturation control. Left: maximum sensitivity $\max_{\phi} d[P/(1+P)]/dP$ along the homogeneous limit cycle as a function of the IP₃ degradation rate λ . The baseline value $\lambda = 0.001$ lies in a strongly saturated regime. Right: finite- k phase-wave speed correction $v_{\phi} - v_{\text{kin}}$ as a function of IP₃ diffusion δ_P for representative values of λ . The baseline sweep is essentially flat, whereas greater δ_P dependence becomes resolvable in less-saturated regimes.

S2. Broad reaction-parameter robustness of the oscillatory amplitude

Figure S2 retains the broad reaction-parameter robustness check separately from the main-text phase-wave speed analysis. The homogeneous calcium oscillation amplitude is mapped over the calcium-release rate α and the calcium-to-IP₃ feedback rate ρ , with $\beta = 0.26$, $\varepsilon_H = 70$, and the remaining parameters fixed at their baseline values. For each value of ρ , the finite-amplitude cycle at $\alpha = 3.5$ was initialized from the baseline oscillatory state, and the solution branch was continued in α in both directions. The amplitude is defined as $\max C - \min C$ over a late-time sampling window. This map is used only to document the persistence and organization of the finite-amplitude oscillatory regime; the direct evidence for reaction-parameter control of the phase-wave speed is provided by the period–speed comparison in Figure 8 of the main manuscript.

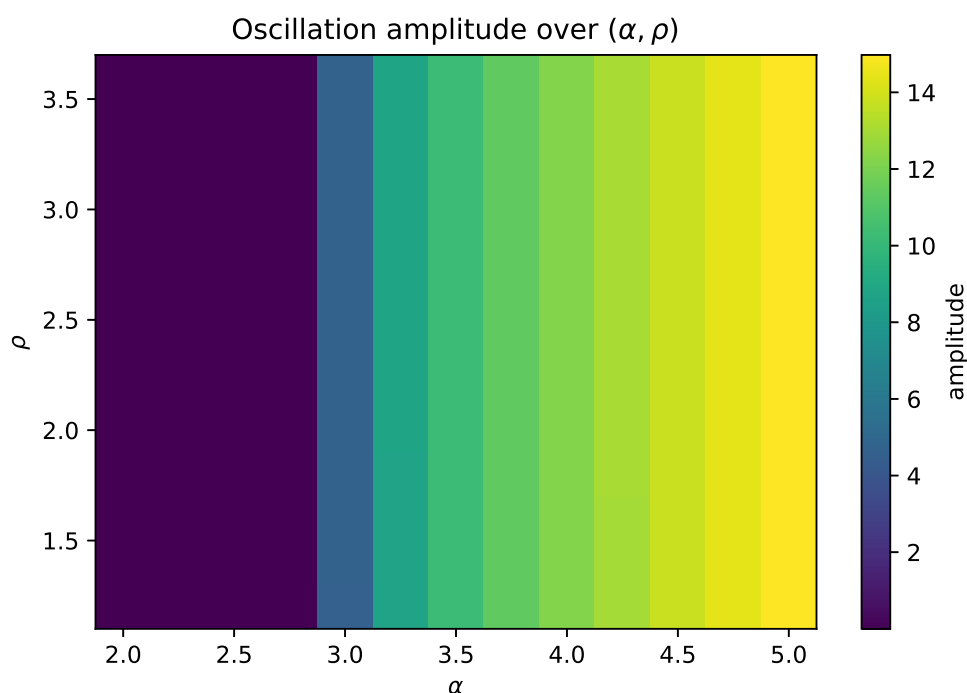


Figure S2. Homogeneous calcium oscillation amplitude over the reaction-parameter plane (α, ρ) at $\beta = 0.26$ and $\varepsilon_H = 70$. The transition from negligible to finite-amplitude oscillations is organized primarily by the calcium-release rate α , while variation in the calcium-to-IP₃ feedback rate ρ has a smaller effect over the tested range.

S3. Numerical robustness near the calcium-diffusion coherence transition

The calcium-diffusion sweep in Figure 5 of the main manuscript assigns a phase-wave speed only when the dominant Fourier mode remains coherent and the phase fit is stationary across the three prescribed late-time windows. To assess the numerical robustness of the change between the last accepted calcium-diffusion point and the first non-coherent point, we repeated the calculations at $\delta_C = 0.05, 0.10$, and 0.20 with $\delta_P = 0.02$ under three numerical settings: the baseline grid and time step, doubled phase-domain resolution, and halved time step. The same acceptance criteria as in the main text were used: $R^2 \geq 0.999$ in all three fitting windows, fitted-speed spread at most 1%, and $\min |A_k| / \text{median } |A_k| \geq 0.20$ over the union of the fitting windows.

Table S2. Transition-region refinement check for the calcium-diffusion sweep at fixed $\delta_P = 0.02$. The column “mode ratio” denotes $\min |A_k| / \text{median } |A_k|$ over the union of the three late-time fitting windows. The classification indicates whether a coherent stationary $m = 1$ phase-wave fit was accepted under the pre-specified screening criteria.

δ_C	setting	N_x^ϕ	Δt	$\min R^2$	phase-wave speed spread (%)	mode ratio	classification
0.05	base	400	10^{-3}	0.999999	0.011	0.98093	coherent
0.05	$2N_x^\phi$	800	10^{-3}	0.999999	0.012	0.98042	coherent
0.05	$\Delta t/2$	400	5×10^{-4}	0.999999	0.011	0.98092	coherent
0.10	base	400	10^{-3}	0.988974	3.985	5.82×10^{-5}	not coherent
0.10	$2N_x^\phi$	800	10^{-3}	0.007625	253.916	8.14×10^{-5}	not coherent
0.10	$\Delta t/2$	400	5×10^{-4}	0.988973	3.962	5.84×10^{-5}	not coherent
0.20	base	400	10^{-3}	0.793071	50.048	2.25×10^{-5}	not coherent
0.20	$2N_x^\phi$	800	10^{-3}	0.793012	50.070	1.73×10^{-5}	not coherent
0.20	$\Delta t/2$	400	5×10^{-4}	0.793071	50.051	6.08×10^{-6}	not coherent

The classification is stable under both refinements. All three runs at $\delta_C = 0.05$ remain coherent, and the relative variation of the accepted v_ϕ values across the three numerical settings is 0.0041%. All runs at $\delta_C = 0.10$ and 0.20 are classified as not coherent; in these cases the dominant-mode amplitude ratio collapses to $O(10^{-5})$ and/or the phase-linearity criteria fail. Thus the classification changes between the tested values $\delta_C = 0.05$ and 0.10. The calculation supports numerical robustness of this interval but is not interpreted as determining a sharp critical diffusion coefficient.

S4. Auxiliary threshold-front diagnostic and numerical refinement checks

For the localized no-flux simulations, an auxiliary threshold-front diagnostic is used only to check the front-tracking implementation. Let C_{rest} be the resting calcium level and C_{max} the maximum attained during the localized response. For a fixed $0 < \eta < 1$, define

$$C_{\text{th}} = C_{\text{rest}} + \eta(C_{\text{max}} - C_{\text{rest}}), \quad x_f(t) = \sup\{x \in [0, 1] : C(x, t) \geq C_{\text{th}}\}.$$

The reported check uses $\eta = 0.5$ and

$$v_{\text{th}} = \frac{x_f(t_2) - x_f(t_1)}{t_2 - t_1},$$

where t_1 and t_2 are selected after the stimulus-induced transient and before boundary interaction. Because v_{th} depends on the threshold and fitting interval, it is confined to this implementation check; the primary propagation quantity in the main study is the phase-wave speed v_ϕ .

The main phase-gradient computations use $N_x^\phi = 400$ and $\Delta t = 10^{-3}$. The baseline calculation was repeated on $N_x^\phi = 200, 400$, and 800 grids and with $\Delta t = 2.5 \times 10^{-4}, 5 \times 10^{-4}, 10^{-3}$, and 2×10^{-3} . The measured v_ϕ changes by less than 10^{-6} in relative terms between $N_x^\phi = 400$ and 800 and remains nearly constant under the displayed time-step refinements. The auxiliary v_{th} changes by less than 1% over $N_x = 200$ –800. These are empirical refinement checks rather than a mathematical convergence proof.

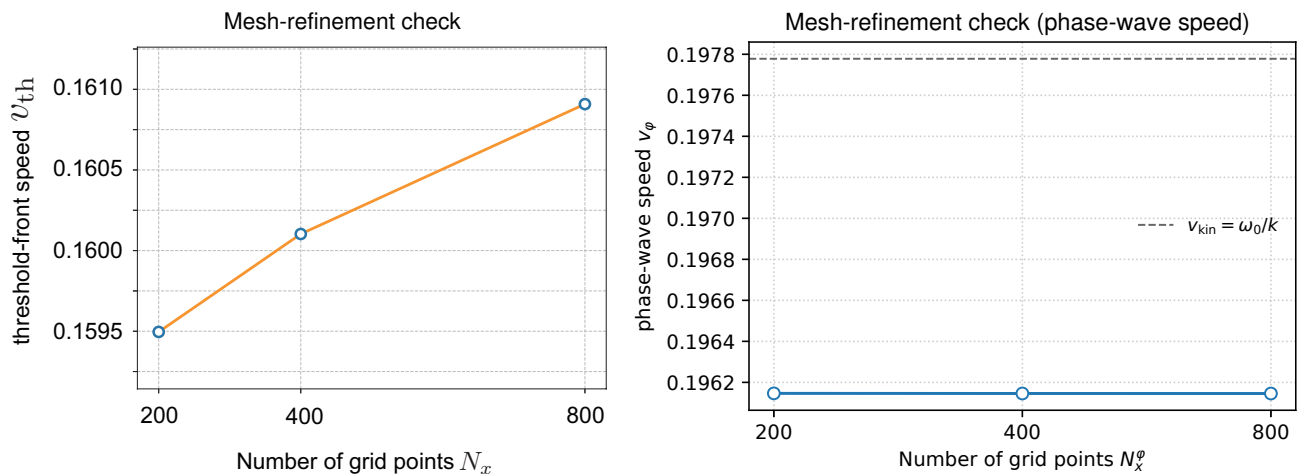


Figure S3. Mesh-refinement checks with 200, 400, and 800 grid points. Left: the auxiliary threshold-front diagnostic v_{th} for the localized no-flux problem. Right: the phase-wave speed v_ϕ for the periodic phase-gradient problem at $L_\phi = 40$ and $m = 1$; the dashed line marks $v_{kin} = \omega_0/k$. The diagnostics are shown separately because they use different initial data, boundary conditions, and measurement rules.

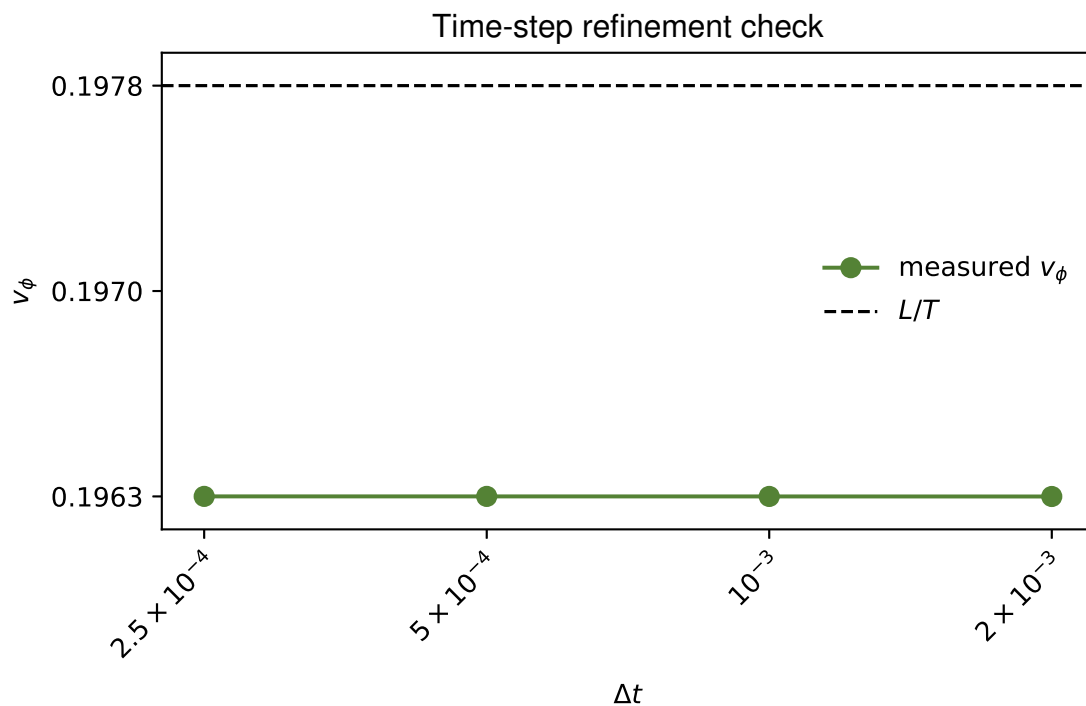


Figure S4. Time-step refinement check for the phase-wave speed v_ϕ at $\delta_C = \delta_P = 0.02$. The measured values remain nearly constant over the displayed time steps; the dashed line denotes the kinematic reference $v_{kin} = \omega_0/k$.

S5. Fisher–KPP front-tracking control

As a separate implementation control, we solve

$$u_t = Du_{xx} + ru(1 - u), \quad r = 1,$$

with a localized front-like initial condition and track a fixed concentration level after the initial transient. The classical minimal front speed is $v_* = 2\sqrt{Dr}$. The computation recovers this scaling over the tested diffusion interval, including a log–log slope close to $1/2$. This control documents the finite-difference/front-tracking implementation for a monostable invasion problem; the phase-wave speed v_ϕ is analyzed independently in the main manuscript.

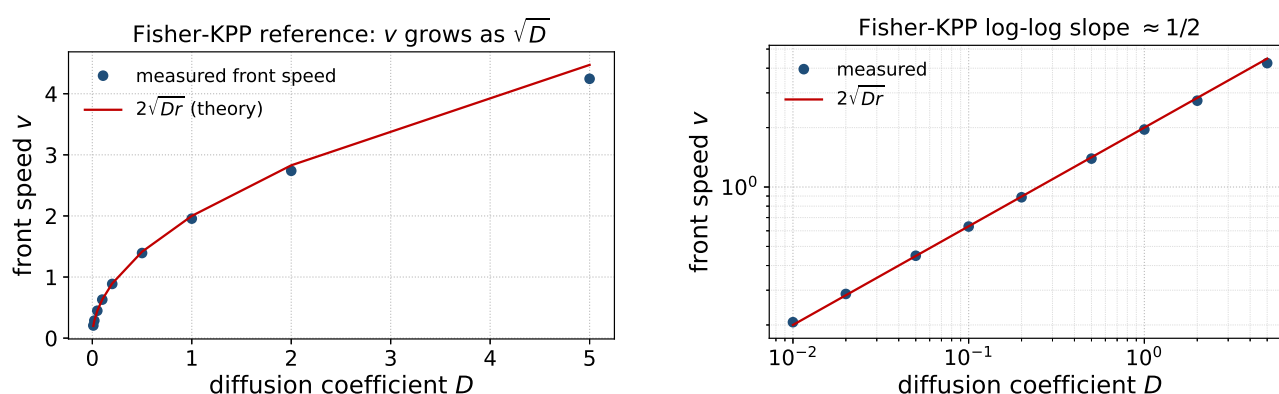


Figure S5. Fisher–KPP front-tracking control. Left: measured front speed and the classical reference $2\sqrt{Dr}$. Right: log–log representation with slope close to $1/2$.



© 2026 the Author(s), licensee AIMS Press. This is an open access article distributed under the terms of the Creative Commons Attribution License (<https://creativecommons.org/licenses/by/4.0>)