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Delayed loss of stability due to the slow passage through Hopf bifurcations in reaction–diffusion equations

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This article presents the delayed loss of stability due to slow passage through Hopf bifurcations in reaction–diffusion equations with slowly-varying parameters, generalizing a well-known result about delayed Hopf bifurcations in analytic ordinary differential equations to spatially-extended systems. We focus on the Hodgkin-Huxley partial differential equation (PDE), the cubic Complex Ginzburg-Landau PDE as an equation in its own right, the Brusselator PDE, and a spatially-extended model of a pituitary clonal cell line. Solutions which are attracted to quasi-stationary states (QSS) sufficiently before the Hopf bifurcations remain near the QSS for long times after the states have become repelling, resulting in a significant delay in the loss of stability and the onset of oscillations. Moreover, the oscillations have large amplitude at onset, and may be spatially homogeneous or inhomogeneous. Space-time boundaries are identified that act as buffer curves beyond which solutions cannot remain near the repelling QSS, and hence before which the delayed onset of oscillations must occur, irrespective of initial conditions. In addition, a method is developed to derive the asymptotic formulas for the buffer curves, and the asymptotics agree well with the numerically observed onset in the Complex Ginzburg-Landau (CGL) equation. We also find that the first-onset sites act as a novel pulse generation mechanism for spatio-temporal oscillations. Published by AIP Publishing. https://doi.org/10.1063/1.5050508

In analytic ordinary differential equations (ODEs), it is known that the onset of oscillations can be significantly delayed when the bifurcation parameter slowly passes through a Hopf bifurcation. This phenomenon is known as delayed stability loss and referred to as delayed Hopf bifurcation. In this article, we report on the discovery that delayed stability loss due to slow passage through Hopf bifurcations also occurs in reaction-diffusion PDEs. We show that delayed Hopf bifurcations naturally arise in a series of paradigm PDEs including the Hodgkin-Huxley PDEs, the Complex Ginzburg-Landau equation, the Brusselator PDEs, and a spatially-extended pituitary lactotroph model. For these systems, the delayed loss of stability impacts the frequency and amplitude of the observed oscillations, and can create a novel pulse-generating mechanism. Moreover, we discover that there is a natural buffer curve in the space-time plane along which solutions must leave a neighborhood of the repelling state. We perform the first analytical calculation of this buffer curve on the Complex Ginzburg-Landau equation, finding excellent agreement with the numerics.

I. INTRODUCTION

Delayed loss of stability is well-established for slow passage through Hopf bifurcations in analytic ordinary differential equations (ODEs). Solutions that start near stable quasi-stationary states (QSS) cross the Hopf bifurcation points and remain near the QSS for long times after they have become unstable, resulting in substantial delays in the onset of oscillations. Moreover, the oscillations have large amplitude at onset. Applications arise in a broad array of disciplines, including chemical reactions, neuroscience, pattern formation, and climate modeling.

In this article, we report on the discovery of delayed loss of stability due to slow passage through Hopf bifurcations (HBs) in reaction-diffusion equations. We focus on a series of four examples which establish the biological, physical, and chemical significance of DHB in spatially extended systems. These include the Hodgkin-Huxley (HH) model which is fundamental in mathematical and computational neuroscience, the cubic Complex Ginzburg-Landau (CGL) equation as an equation in its own right, the Brusselator which is central to pattern formation, and a spatially-extended model of a pituitary lactotroph clonal cell line.

With slowly-varying parameters, these partial differential equations (PDEs) exhibit delayed loss of stability due to the slow passage through Hopf bifurcations, and we label this delay by DHB. We first identify conditions in which the delayed onset of the instability is spatially homogeneous, and compare to known results for DHB in ODEs. Then, we report on the rich dynamics observed when the delayed onset is spatially inhomogeneous, and examine how the inhomogeneities depend on the diffusivity and the source terms. In particular, we begin by presenting the dynamics of both spatially homogeneous and inhomogeneous DHB for the paradigm HH PDEs and for the canonical CGL equation.

Next, a method is developed to derive asymptotic formulas to predict when solutions must diverge exponentially from the unstable QSS. These give buffer curves in the space-time plane past which solutions with initial...
conditions sufficiently far from the HB on the stable side cannot remain near the unstable QSS, and along which the delayed onset of oscillations must occur. We also show that, for CGL, the analytically-determined buffer curves agree with the onset curves obtained from simulations over a wide range of (complex) diffusivities.

After presenting the new phenomenon of DHB in the context of the canonical HH and CGL equations and shown analytically that there are buffer curves which predict the spatial dependence of the DHB phenomenon, we next turn to establish its ubiquity. In particular, we study spatially homogeneous DHB in the canonical Brusselator system from chemical pattern formation theory. Also, we show that DHB occurs naturally in a neuroendocrine example consisting of a pituitary lactotroph cell line, for which there is considerable information establishing the relation between experimentally controlled quantities and parameters in the model. In this manner, we provide motivation for some new neuroscience experiments.

Finally, we report on the discovery of a novel pulse-generating mechanism created by DHB. We illustrate this in the HH PDEs and in the CGL equation.

In addition to studying DHB in the four main PDE models, we also discovered DHB in other reaction–diffusion systems with source terms, including the FitzHugh-Nagumo,36 Morris-Lecar,36 and Hindmarsh-Rose37 PDEs, finding homogeneous and inhomogeneous delayed loss of stability and pulse generators (not shown).

II. DELAYED STABILITY LOSS IN HH

DHB occurs in the HH model with a slowly ramped applied current, \( I \),

\[
C_m v_I = I - (I_{Na} + I_K + I_L) + I_a(x) + \varepsilon D v_{xx},
\]

\[
\xi = \alpha_\xi(\nu)(1 - \xi) - \beta_\xi(\nu)\xi,
\]

\[
I_L = \varepsilon,
\]

where \( \nu \) is the membrane potential of the cell, \( \xi \in \{m,n,h\} \) denotes the gating variables, and \( x \) is the position along the axon. The small diffusion coefficient, \( \varepsilon D \), corresponds to thin axons. The ionic currents and the functions \( \alpha_\xi \) and \( \beta_\xi \) are given in Ref. 21. Unless stated otherwise, the parameters have the values listed in Ref. 21, together with \( \varepsilon = 0.01 \) and \( D = 0.5 \).

The fast subsystem \([\varepsilon \to 0 \text{ in } (1)]\) possesses spatially-dependent, hyperpolarized QSS given to leading order by

\[
I = I_{Na} + I_K + I_L - I_a(x),
\]

where \( \xi = \frac{\alpha_\xi(\nu)}{\alpha_\xi(\nu) + \beta_\xi(\nu)} \). The higher order terms of the QSS of \((1)\) can be calculated by using \( I \) as the slow time, and substituting the asymptotic series expansion \( \rho(x,I) = \rho_0(x,I) + \varepsilon \rho_1(x,I) + O(\varepsilon^2) \), where \( \rho \in \{v,m,n,h\} \). The leading order terms, \( \rho_0 \), are given by \((2)\). The \( O(\varepsilon) \) corrections are the solutions of the linear system

\[
(\nabla(I_{Na} + I_K + I_L) \cdot (v_I, m_I, n_I, h_I))^T = D v_{0,xx} - C_m v_{0,x} \\
[\alpha_\xi - (\alpha_\xi + \beta_\xi)\xi] v_I - (\alpha_\xi + \beta_\xi)\xi_I = \xi_0,\]

where \( \nabla \) is the gradient with respect to \((v,m,n,h)\), the derivatives of \( v_I \) and \( \xi_0 \) are obtained by differentiation of \((2)\), and all functions are evaluated at \( \rho_0(x,I) \). These QSS are stable for each fixed \( I \) up to small positive \( I \), and change stability along spatially inhomogeneous curves, \( \mathcal{H} \), of HB. The frequency along \( \mathcal{H} \), however, is independent of \( x \).

With \( 0 < \varepsilon \ll 1 \), solutions of \((1)\) pass through \( \mathcal{H} \) due to the slow drift in \( I \), and there is delayed loss of stability. We classified solutions as having switched from QSS to oscillations when the distance from the QSS exceeds \( \sqrt{\varepsilon} \).

For spatially homogeneous sources, solutions with initial conditions sufficiently far from \( \mathcal{H} \) escape the neighbourhood of the QSS, given by \((2)\) to leading order, and begin oscillating at \( I \approx 10.3 \) in a uniform manner. This value of \( I \) is the maximal delay observed in the space-clamped HH equations \([\{1\} \text{ with } D = 0]\). The uniformity of the stability loss (for any \( D \)) is due to the homogeneity of both \( I_a(x) \) and the frequency along \( \mathcal{H} \).

Inhomogeneous \( I_a(x) \) induce spatially inhomogeneous delayed stability loss in HH \([\text{Figs. 1(a)–1(c)}]\). With \( I(0) \) sufficiently far from \( \mathcal{H} \) to eliminate memory effects, the instability first manifests near the maxima of \( I_a(x) \). The delay in the stability loss is longer where \( I_a(x) \) is more negative.

For a Gaussian source with \( a = 5 \) and \( \sigma = 5 \), we measured the distance, \( I_{\text{onset}} - I_{\text{HB}} \), that solutions stayed close to the QSS, given by \((2)\) to leading order, past \( \mathcal{H} \) [Fig. 1(d)]. For \( D = 0 \), the delay is almost spatially uniform (red curve). The minor variations are due to the numerical sensitivity associated with using initial value solvers to follow unstable QSS—more precise measurements can be made by constructing solutions using boundary value solvers (not shown). For small \( D \), the instability that first sets in at \( x = 0 \) spreads locally, but has no long-range effect (green curve). This results in a pair of minima in the delay curve, while the edges remain close to the ODE values. For larger \( D \), the onset curve widens and solutions with large \( |x| \) escape much sooner than their ODE counterparts (blue curve).

Here, we observe that spatially localized current sources, \( I_a(x) \), such as Gaussians, arise naturally in neuroscience. For example, EEG data from the primary auditory cortex in certain primates exhibits spatially localized current source densities.38 Locally generated intracortical synaptic currents exhibit tapered peaks at (supra)granular sites (see figure 2 in Ref. 38). Other experiments and models have identified the importance of treating cortex as a spatially inhomogeneous medium, with localized synaptic currents.

III. DELAYED STABILITY LOSS IN CGL

DHB also occurs in CGL with source term, \( I_a(x) \), and slowly varying parameter,

\[
\mu_\nu = \nu + i\omega_\nu A + \varepsilon D v_{xx} + \sqrt{\varepsilon} I_a(x) - \alpha |A|^2 A,
\]

where \( \alpha = 1 + i\omega_\nu \) is the nonlinear frequency, \( D = \beta_\nu + i\beta_\nu \) is the
linear dispersion,39,40 and $0 < \varepsilon \ll 1$ measures the timescale separation. Here, we have set the amplitude of the source term to be $O(\sqrt{\varepsilon})$ and that of the diffusivity to be $O(\varepsilon)$ for convenience of the analysis. Below, we show that the results may be extended separately to the cases of large-amplitude source terms [up to $O(1/\sqrt{\varepsilon})$] and of $O(1)$ diffusivity, respectively.

Simulations of (3) were performed with zero-flux boundary conditions on $[-L, L]$ for a range of $L$ values. All numerical simulations were performed using balanced symmetric Strang operator splitting,41,42 with centered finite differences for the Laplacian and fourth-order Runge-Kutta for the time stepping. The discretization was chosen fine enough to resolve all modes up to those with $k = O(e^{-3/2})$. We verified our numerical results using a second-order Crank-Nicolson scheme and found good agreement between the independent methods. On sufficiently large domains, we observe similar results for the onset of oscillations with Dirichlet boundary conditions. Unless stated otherwise, $\varepsilon = 0.01, \omega_0 = 0.5, \alpha_r = 0.6, \beta_r = 1$, and $\beta_i = 0$.

In the singular limit $\varepsilon \rightarrow 0$, (3) is the normal form for a supercritical HB. If $\mu < 0$ (below criticality), $A \equiv 0$ is stable. If $\mu > 0$ (above criticality), $A \equiv 0$ is unstable. For $\mu = 0$, the system undergoes a supercritical HB with frequency $\omega_0$. With $0 < \varepsilon \ll 1$, the slow increase of $\mu$ causes (3) to pass through the curve, $\mathcal{H}$, of HB (Fig. 2).

For spatially homogeneous sources, $I_\mu(x) = a, a \in \mathbb{R}$, the transition from QSS to temporal oscillations occurs uniformly at approximately $\mu = 0.5$ [Fig. 2(a)], which is the frequency, $\omega_0$, and is the maximal delay time predicted by the theory of slow passage through HB in ODEs.1-6,43 which applies in this case of homogeneous sources. Constant source terms arise in spatially-resonant traveling wave forcing of the CGL equation for $1 : m$ resonances, e.g., Refs. 44 and 45.

For Gaussian sources [$I_\mu(x) = a \exp(-x^2/2)$], the instability first occurs at $x = 0$, where $|I_\mu(x)|$ takes its maximum, at time $\mu = \omega_0$. For larger $|x|$, the onset of oscillations occurs for later $\mu$ making the delay longer and spatially inhomogeneous [Fig. 2(b)], and defining the onset curve in the $(\mu, x)$ plane. For mollified step sources [$I_\mu(x) = \frac{1}{2} a (1 + \tanh x)$], the instability first occurs along $x \geq 0$ where $|I_\mu(x)|$ takes its maximum, at time $\mu = \omega_0$. For an inverted mollified bump source ($I_\mu(x) = \frac{1}{2} a [1 - \frac{1}{2} \tanh(x + x_0) - \tanh(x - x_0)]$), the onset curve is spatially uniform for $|x| \gtrsim 25$, and is spatially-dependent for $|x| \lesssim 25$, exhibiting the longest delay at $x = 0$ [Fig. 2(d)].

In all cases, the system remains close to its QSS (green background) well past $\mathcal{H}$. For general $I_\mu(x)$, the QSS is

$$A = -\frac{I_\mu(x)}{\mu + i \omega_0} \sqrt{\varepsilon} + \left[\frac{I_\mu(x)}{\mu + i \omega_0} + D(\mu + i \omega_0)I''_\mu(x)
\left.\vphantom{\frac{1}{\mu + i \omega_0}}\right|_{\mu + \omega_0}(\mu + i \omega_0)\right]^{3/2} + O(\varepsilon^{5/2}).$$

A representative solution—with time series for five different values of $x$—is shown in Fig. 3, along with the QSS for a Gaussian source. Simulations with other sources also show that solutions stay close to the QSS well past $\mathcal{H}$.

A. Buffer curves of (3) in the $(\mu, x)$ plane

There are buffer curves in the $(\mu, x)$ plane past which solutions of (3) cannot stay near the repelling QSS, for any $\mu_0 < -\omega_0$. For general $I_\mu(x)$, the buffer curves are derived by Fourier analysis of the linearization about the QSS,

$$\varepsilon \hat{A}_\mu = (\mu + i \omega_0 - \varepsilon Dk^2) \hat{A} + \sqrt{\varepsilon} I_\mu(k),$$

FIG. 1. Solutions of the HH equations (1) stay close to the QSS [blue background; Eq. (2) to leading order] beyond $\mathcal{H}$ and transition to action potentials at the (yellow) onset curve for (a) $D = 0$, (b) $D = 0.2$, and (c) $D = 5$. (d) Temporal delay (I-distance between onset and HB curves) for $D = 0$ (red), $D = 0.2$ (green), and $D = 5$ (blue).

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\left.\vphantom{\frac{1}{\mu + i \omega_0}}\right|_{\mu + \omega_0}(\mu + i \omega_0)\right]^{3/2} + O(\varepsilon^{5/2}).$$

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where $\hat{A}$ is the Fourier transform of $A$. With initial condition $\hat{A}(\mu_0, k) = \hat{A}_0$, the solution of (5) has homogeneous part,

$$\hat{A}_{\text{hom}} = \hat{A}_0 \exp \left[ \frac{1}{2} (\mu - \mu_0)(\mu + \mu_0 + 2i\omega_0 - 2\epsilon Dk^2) \right],$$

and inhomogeneous part

$$\hat{A}_{\text{inhom}} = \sqrt{\frac{\pi}{2}} L_\sigma(k) \exp \left[ \frac{(\mu + i\omega_0 - \epsilon Dk^2)^2}{2\epsilon} \right] \times \left[ \text{erf} \left( \frac{\mu + i\omega_0 - \epsilon Dk^2}{\sqrt{2\epsilon}} \right) - \text{erf} \left( \frac{\mu_0 + i\omega_0 - \epsilon Dk^2}{\sqrt{2\epsilon}} \right) \right].$$

Here, erf is the error function, $\text{erf}(z) = \frac{2}{\sqrt{\pi}} \int_0^z e^{-t^2} \, dt$. Fourier inversion shows that $A_{\text{hom}}$ is

$$A(x, \mu_0) \sqrt{2D(\mu - \mu_0)} * \exp \left[ \frac{(\mu - \mu_0)(\mu + \mu_0 + 2i\omega_0) - x^2}{4D(\mu - \mu_0)} \right].$$

(6)

where the asterisk denotes the convolution. Similarly, $A_{\text{inhom}}$ is asymptotically proportional to

$$I_\sigma(x) * \exp \left[ \frac{(\mu + i\omega_0)^2}{2\epsilon} - \frac{x^2}{4D(\mu + i\omega_0)} \right],$$

(7)

neglecting $O(\epsilon^2 D^2 k^4)$ and higher order terms.

The buffer curves are determined by (7). For initial conditions with $\mu_0 < -\omega_0$, both (6) and (7) remain exponentially small (in $\epsilon$) until at least $\mu = \omega_0$. Moreover, (7) grows exponentially before (6) does. Therefore, the curve in the $(\mu, x)$ plane along which (7) first begins to grow exponentially is the buffer curve past which solutions cannot remain near the repelling QSS. Spatially decaying sources can balance the temporal exponential growth in (7) and hence further delay the onset to oscillations.

**B. Buffer curves of (3) for Gaussian sources**

Evaluation of (7) for a Gaussian source gives a term proportional to

$$\exp \left[ \frac{(\mu + i\omega_0)^2}{2\epsilon} - \frac{x^2}{4[\sigma + D(\mu + i\omega_0)]} \right].$$

(8)
and the delay becomes more spatially uniform.

At $O(\varepsilon^2)$, (9) is unchanged. Fig. 4(c) demonstrates the effectiveness of the asymptotics for a Gaussian source with $a = 100$, so that the inhomogeneity in (3) is $O(\varepsilon^{-1/2})$. In Fig. 4(c), the red pencil at the nose of the buffer curve corresponds to the large-amplitude QSS.

C. Large-amplitude sources in (3)

The sources in (3) have $O(\sqrt{\varepsilon})$-amplitude as a convenience for analysis. For larger amplitudes, even up to $O(\varepsilon^{-1/2})$, the QSS is a nonlinear function of $I_a(x)$. Linearization about the QSS shows that delayed stability loss persists, and (9) is unchanged. Fig. 4(c) demonstrates the effectiveness of the asymptotics for a Gaussian source with $a = 100$, so that the inhomogeneity in (3) is $O(\varepsilon^{-1/2})$. In Fig. 4(c), the red pencil at the nose of the buffer curve corresponds to the large-amplitude QSS.

D. $O(1)$ diffusivities in (3)

The analysis of weak diffusion, $\varepsilon D$, may be extended to $\varepsilon D = O(1)$ provided the source amplitudes are $O(\sqrt{\varepsilon})$. Linearizing about the trivial state, we find that (9) with $\sigma \to \varepsilon \sigma$ and $x \to \sqrt{\varepsilon} x$ gives the buffer curve, which agrees with the numerics (Fig. 5).

IV. DHB IN THE BRUSSELATOR WITH SLOWLY VARYING PARAMETER

DHB occurs in the Brusselator model for autocatalytic reactions with slowly varying parameter,

$$u_t = a - (1 + b) u + w^2 v + \varepsilon D_\lambda \partial_x u - \sqrt{\varepsilon} I_\mu(x),$$

where $D_\lambda$ depends on the reaction parameter $\lambda$. The source in (3) is a reaction with slowly varying parameter, $\mu = \lambda t$. Thus, the constant mode is the first to cause the solution to diverge from the unstable QSS, consistent with (9).

For initial conditions with $-\omega_0 < \mu_0 < 0$, (6) diverges exponentially before (7). Hence, solutions with $\mu_0$ sufficiently close to $\mu$ will transition to oscillations relatively early (near $\mu = -\mu_0$) and not experience maximal delay. This is known in ODEs as a memory effect.$^2,^3,^4$
FIG. 5. DHB in (3) with (a) $\varepsilon D = O(1)$ and $O(\sqrt{\varepsilon})$-amplitude source term; $(\beta_1, \beta_2, a) = (100, 0, 1)$, and (b) $\varepsilon D = O(1)$ and $O(1)$-amplitude source term; $(\beta_1, \beta_2, a) = (100, 0, 35)$. The (black) buffer curve (9) still provides a good approximation of the onset curve. The red pencil at the nose in (b) is due to the large-amplitude QSS.

\begin{align*}
v_t &= bu - u^2v + \varepsilon Du v_{xx} - \sqrt{\varepsilon} I_c(x), \\
b_t &= \varepsilon. 
\end{align*}

Here, $u$ and $v$ denote the concentrations of the two species, $a$ is the growth rate of the concentration of the first species (it is the constant concentration of a substrate that is converted into the first species), and $b$ is the concentration of another substrate. The small-amplitude Gaussian forcing terms, $I_a$ and $I_v$, represent weak light sources, and we again assume weak diffusivities, $\varepsilon D_a$ and $\varepsilon D_v$, for convenience.

System (10) possesses QSS given by \((u,v) = \left(a - \sqrt{\varepsilon}(I_a + I_v) + O(\varepsilon), \frac{\varepsilon}{\sqrt{\varepsilon}}(bI_a + (b-1)I_v) + O(\varepsilon)\right)\). These QSS undergo HB along $b = b_H(a, x, \varepsilon)$, where

$$b_H(a, x, \varepsilon) = 1 + a^2 + 2\sqrt{\varepsilon} \left[ \left( \frac{1}{a} - a \right) I_v(x) - a I_a(x) \right] + O(\varepsilon)$$

and Turing bifurcations along $b = (1 + \sqrt{D_v D_a})^2 + O(\sqrt{\varepsilon}) : 0 < \frac{D_v}{D_a} < 1$, with critical wave number given by $\kappa_c^2 = a/(\varepsilon \sqrt{D_v D_a})$, to leading order. Moreover, higher order terms in the expressions for $b$ and $\kappa_c^2$ at the Turing bifurcations on the QSS are readily obtained. We choose the diffusivities and initial conditions such that solutions of (10) encounter the HB well before the Turing instabilities.

With $0 < \varepsilon \ll 1$, the slow increase in $b$ carries solutions through the Hopf curve, resulting in delayed loss of stability (Fig. 6). In addition, we find similar dependence of the delay on the diffusivity and forcing as in the HH and CGL equations, i.e., the delay is shortest at the center of the domain (where the forcing has largest magnitude). Moreover, the delay at the center is consistent with the ODE case, where we note that the natural frequency, $\omega_0$, at the HB is $\omega_0^2 = a^2 - 2a\sqrt{\varepsilon} [I_a(x) + I_v(x)] + O(\varepsilon)$. In particular, with $a = 1$ and the other parameters set as in Fig. 6, the observed delay at the center is approximately the natural frequency. In addition, an increase in the magnitude of the diffusivity amplifies the long-range effect of the delay (not shown).

V. DHB IN A PITUITARY CELL LINE MODEL

We also observe DHB in a PDE model of the electrical activity in a pituitary lactotroph clonal cell line,

$$C_m V_t = -\sum I_{ionic} + I_{app}(x) + D V_{xx},$$

$$\tau_n n_t = n_{\infty}(V) - n,$$

$$\tau_v e_t = e_{\infty}(V) - e.$$  

The currents are calcium ($I_{Ca}$), delayed rectifier $K^+$ ($I_K$), A-type $K^+$ ($I_A$), and leak ($I_L$). $(V, n, e)$ are the membrane potential and gating variables for $I_K$ activation and $I_A$ inactivation.\cite{33,35} $I$ is a baseline current. The cells (positions $x$) are coupled via gap junctions.

We refer the reader to Ref. 46 for instances of heterogeneity in pituitary clonal cell lines.

We show that (11) exhibits DHB with baseline current $I = I_0 - \varepsilon t$. As $\varepsilon \to 0$, (11) with $\varepsilon = 0$ possesses depolarized QSS (Fig. 7: red) given by $I = \sum I_{ionic} - I_{app}(x)$, where $n = n_{\infty}(V)$ and $e = e_{\infty}(V)$. The stable and unstable parts of the QSS are separated by a curve, $\mathcal{H}$, of subcritical HB. For $I$ to the right (left) of $\mathcal{H}$, the QSS are stable (unstable, respectively).

With $0 < \varepsilon \ll 1$, solutions with initial data sufficiently far from $\mathcal{H}$ pass through $\mathcal{H}$ due to the slow decrease in $I$ and stay close to the QSS well past $\mathcal{H}$. For homogeneous $I_{app}$,
VI. PULSE GENERATORS IN SYSTEMS WITH SPATIALLY INHOMOGENEOUS DHB

In addition to our discovery of spatio-temporal delayed loss of stability due to slow passage through HB, we found that DHB can create a novel pulse-generating mechanism. We return to the HH PDEs (1) and the CGL equation (3) to illustrate this mechanism.

For the HH PDE (1), we find that spatially-inhomogeneous DHB leads to a novel pulse generation mechanism. Behind the onset curve, the solution at \( x = 0 \) deviates from its QSS [Figs. 8(a) and 8(b)], and then a pair of action potentials rapidly emerge [Figs. 8(c)–8(f)] and spread outward (only solutions escape the neighbourhood of the QSS and oscillate uniformly after a substantial delay, at the value of \( I \) predicted by the ODE. Uniformity (for all \( D \)) is due to the homogeneity of \( I_{\text{app}} \) and the frequency along \( \mathcal{H} \). Inhomogeneous \( I_{\text{app}}(x) \) induce inhomogeneous DHB in (11). The delay is shortest where \( |I_{\text{app}}(x)| \) is maximal, and lengthens as \( |I_{\text{app}}(x)| \) decreases [Figs. 7(a)–7(c)].

For Gaussian sources, the delay, \( |I_{\text{onset}}(x) - I_{\text{HB}}(x)| \), shows that solutions stay close to the QSS past \( \mathcal{H} \) [Fig. 7(d)]. For \( D = 0 \), the delay (red) is almost spatially uniform. For small \( D \) (green), the instability sets in at \( x = 0 \) and spreads until \( |x| \approx 25 \). For larger \( D \) (blue), the delay is shorter.

FIG. 7. DHB in (11) with \( g_K = 4 \) nS, \( g_L = 5 \) nS, \( a = 1 \), and \( \sigma = 50 \). Solutions stay close to the QSS (red) left of \( \mathcal{H} \) and transition to bursts at the yellow onset curve for (a) \( D = 0 \), (b) \( D = 0.001 \), and (c) \( D = 0.02 \). (d) Bifurcation delay.

FIG. 8. Pulse generation due to slow passage through HB in the HH model (1) shown on the interval \( 0 \leq x \leq \frac{L}{5} \).
the rightward traveling waves are shown). Once the newly-formed action potentials are sufficiently far from \( x = 0 \), the process repeats, adding pulses to the propagating waveform.

Pulse generators also arise in the CGL equation (3). Since the instability first sets in where \( |I_a(x)| \) has a local maximum, these are the points where the solutions first approach the stable limit cycles. Pulses generated at such sites propagate away from them in space. For the Gaussian sources, pairs of outward propagating pulses are generated at \( x = 0 \); the pulse dynamics may be seen from the colors in Figs. 2 and 4. For the inverted mollified bump, inward propagating pulses are generated at the edges of the domain, and they interfere destructively at \( x = 0 \) [Fig. 2(d)]. After a transient, the pulse generation at the edges of the domain balances the destructive interference at the origin so that the total number of spatial oscillations is invariant. Therefore, for various different types of inhomogeneous sources, slow passage through HB also creates a novel pulse-generation mechanism. Moreover, the speed of the pulses may be calculated from (9) using implicit differentiation to find \( \frac{\partial u}{\partial p} \).

VII. SUMMARY

We reported on the discovery of spatially homogeneous and inhomogeneous delayed stability loss due to slow passage through Hopf bifurcations, labelled DHB, in the Hodgkin-Huxley PDEs with a slowly ramped applied current, the Complex Ginzburg-Landau equation with slowly-varying linear growth rate, the Brusselator with slowly varying intermediate species, and a pituitary lactotroph cell line model with slowly varying applied current. We developed a method to derive asymptotics for the buffer curves where solutions transition from QSS to oscillatory states. Moreover, our results extend beyond small-amplitude inhomogeneities; delayed stability loss persists in CGL and HH with \( \mathcal{O}(\varepsilon^{-1/2}) \) and \( \mathcal{O}(1) \) inhomogeneities, respectively, as well as to \( \mathcal{O}(1) \) diffusivity in the CGL equation. Finally, we showed that DHB creates a novel pulse generation mechanism, and (data not shown) we found similar results in the FitzHugh-Nagumo, Hindmarsh-Rose, and Morris-Lecar models with diffusion and source terms; some analysis of the FitzHugh-Nagumo PDE is given in Ref. 48.

In formally deriving the buffer curve formula, we have only used the linear terms in the PDE. This is suggested by the analysis of DHB in analytic ODEs. There, the linear terms determine the locations of the buffer points to leading order and hence the maximal length of the delay, and the nonlinear terms are higher order, see Refs. 2 and 6. Here, for PDEs, the good agreement between the buffer curve analysis and the numerically-observed onset of oscillations, as well as preliminary analysis, also suggest that the nonlinear terms only have higher order effects, as well. This is the subject of ongoing work.

In chemical systems, such as the Brusselator and BZ reactions, there are applied, spatially-localized light sources. Slow passage through HB in these systems might be studied using the approach developed here. Also, the new results for delayed onset of oscillations will be useful for control in spatially extended systems with HB, suggesting a possible mechanism to suppress the oscillations in part of the parameter regime where they would otherwise naturally arise. Moreover, this analysis will provide insights for analyzing slow passage of pulses through instabilities in activator-inhibitor systems, Ref. 49.

The dynamical systems analogs of the QSS are invariant slow manifolds. Hence, our results motivate rigorously determining whether or not there exist invariant manifolds and, if so, measuring their splitting distance in these PDEs. The results also motivate rigorous analysis of other delayed bifurcation phenomena including canards in spatially extended media. Canards are solutions of multi-scale ODEs that closely follow attracting QSS across a fold bifurcation and remain close to repelling QSS for long times. They explain the sudden change in amplitude and period of oscillations in chemical reactions, 30 and the firing patterns of excitable cells. 31

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43 The minor variations are due to the numerical sensitivity associated with using initial value solvers to follow unstable QSS – more precise measurements can be made by using boundary value solvers.


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