



SPATIAL HETEROGENEITY LOCALIZES TURING PATTERNS IN REACTION-CROSS-DIFFUSION SYSTEMS

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ABSTRACT. Motivated by bacterial chemotaxis and multi-species ecological interactions in heterogeneous environments, we study a general one-dimensional reaction-cross-diffusion system in the presence of spatial heterogeneity in both transport and reaction terms. Under a suitable asymptotic assumption that the transport is slow over the domain, while gradients in the reaction heterogeneity are not too sharp, we study the stability of a heterogeneous steady state approximated by the system in the absence of transport. Using a WKB ansatz, we find that this steady state can undergo a Turing-type instability in subsets of the domain, leading to the formation of localized patterns. The boundaries of the pattern-forming regions are given asymptotically by ‘local’ Turing conditions corresponding to a spatially homogeneous analysis parameterized by the spatial variable. We developed a general open-source code which is freely available, and show numerical examples of this localized pattern formation in a Schnakenberg cross-diffusion system, a Keller-Segel chemotaxis model, and the Shigesada-Kawasaki-Teramoto model with heterogeneous parameters. We numerically show that the patterns may undergo secondary instabilities leading to spatiotemporal movement of spikes, though these remain approximately within the asymptotically predicted localized regions. This theory can elegantly differentiate between spatial structure due to background heterogeneity, from spatial patterns emergent from Turing-type instabilities.

Dedication. We would like to dedicate this paper to the memory of Professor Masayasu (Mayan) Mimura, one of the pioneers of mathematical biology. Not only was Mayan an exceptional mathematician, he would also enthusiastically encourage others and was particularly kind and generous to early career researchers. He always brought a smile to every face.

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1. **Introduction.** A major extension to Turing's Chemical Theory of Morphogenesis [40] is the incorporation of transport beyond Fickian diffusion such as models of chemotaxis [13, 11, 10] and general cross-diffusion [28, 6, 25, 35, 8, 33]. While the basic ideas of linear stability analysis employed by Turing to predict pattern formation in reaction-diffusion systems extends readily to such systems [29, 19], the inclusion of spatial heterogeneity leads to difficulties in predicting pattern formation using linear analysis. Yet even Turing himself was well-aware that few biological systems actually form spontaneous spatially-structured patterns from purely homogeneous ones. Rather, most organisms evolve from some complex spatial state to another spatially patterned state during different stages of development. Such 'hierarchical' pattern formation arising from interacting systems on different temporal and spatial scales is likely commonplace in embryonic development [26, 20], with some authors suggesting that such mechanisms can be modelled via cross-diffusion systems [34]. In evolutionary and ecological settings, where cross-diffusion-type interactions are especially well-motivated [30], spatial heterogeneity is extremely important, accounting for innate landscape and demographic variation [5]. In such settings it is especially important to be able to determine if an observed variation in population density is due to environmental heterogeneity, or due to species interactions. In this paper, we develop a theory to predict and understand pattern formation in spatially-heterogeneous cross-diffusion systems, under the assumption of a scale separation between the heterogeneity and the pattern wavelength. Within this asymptotic regime, our theory can distinguish between spatial structure due to background heterogeneity and spatial patterns due to Turing-type instabilities.

Spatial heterogeneities in reaction-diffusion systems have been (numerically) shown to change local instability conditions for pattern formation [3, 31], modulate the size and wavelength of patterns [32], and localize (or pin) spike patterns in space [12, 44, 45], which can be studied analytically for certain systems in a semi-strong interaction regime. The presence of even simple spatial heterogeneity in reaction-diffusion systems can induce spatiotemporal effects, such as changing the stability of patterned states and leading to the movement of spike solutions [21, 14]. In regimes of highly localized spike solutions [12, 44, 45], or highly localized heterogeneities [7], some specific models are analytically tractable. There are some studies on bifurcation structures in spatially-heterogeneous cross-diffusion systems [22, 4] for specific models. Nevertheless, there are few tools for understanding spatially-heterogeneous reaction-(cross)-diffusion systems with the same level of generality, and giving the same level of insight, as Turing's original use of linear stability analysis.

The typical Turing-type linear stability analysis proceeds by first linearizing the model about a spatially homogeneous steady state, and then exploiting eigenvalues of the spatial operators (the Laplacian in the context of general cross-diffusion). Using an eigenfunction (of the Laplacian) and exponential in time ansatz, one can reduce the study of instabilities to the computation of eigenvalues of a given matrix. These eigenvalues then indicate linear (in)stability of a particular eigenfunction, and hence one can develop an idea of what spatial perturbations might grow, and hence form spatially patterned states. In the limit of a sufficiently large domain, one can use the approximation of a continuous spatial spectrum to derive conditions involving only the parameters of the model which are necessary for such pattern-forming instabilities, and which become sufficient on large enough domains [29]. Such conditions are a valuable result from the linear analysis, as they often give

biologically-interpretable insight into general classes of models, such as the celebrated short-range activation/long-range inhibition theory of pattern formation in two-species reaction-diffusion systems [27].

This analysis, however, requires the existence of a spatially homogeneous equilibrium, and the spectral analysis of a scalar operator (the Laplacian). In general spatially-heterogeneous systems, such assumptions are violated. In addition to the difficulties inherent in computing steady states of these spatially-heterogeneous systems, linearization about such a state typically leads to linear systems involving spatial operators coupling multiple species. Theory for such non-scalar Sturm-Liouville problems does exist (see Section 3.1 of [43] for discussion and references), but it is typically not useful for analytical computations as one has to determine the spectrum via numerical approximations anyway. If a spatially-heterogeneous steady state can be found, one can use Galerkin expansions to compute instability conditions by truncating an infinite-matrix system (arising from coupled modes which are ‘diagonalized’ in the homogeneous setting) [16, 42]. However, this analysis is quite involved for a given system, and does not often lead to general biological insights such as those gained by deriving necessary conditions for pattern formation in the homogeneous setting. From a modelling perspective there is also a difficulty in differentiating between spatial structure arising from nonlinear interactions and instability, and spatial structure due to the underlying heterogeneity. As mentioned, determining precisely what causes an observed spatial variation in a population or a developing organism is extremely valuable for mechanistic understanding, and eventually for influencing or controlling the system such as in conservation ecology or tissue engineering.

Recently, in the context of spatial heterogeneity in the kinetics of one-dimensional reaction-diffusion systems, we proposed a theory of linear stability addressing the above challenges [17]. We assumed a separation of scales allowing us to write the model in a limit of asymptotically small transport relative to kinetic interactions. Such a limit in the spatially homogeneous case can be related to assuming a sufficiently large domain so that the spatial spectrum of the Laplacian can be well-approximated as a continuous variable. In this regime, we used a WKB ansatz to study the stability of a heterogeneous steady state, finding that the usual Turing instability conditions could be satisfied locally as if they were simply parameterized by the spatial variable. Such a localization of these conditions was shown to precisely correspond to where full numerical simulations found patterned states deviating from a heterogeneous steady state. Another key insight was that this steady state could be well-approximated by zeros of the reaction kinetics, and hence became analytically amenable in a wide class of systems.

In this paper, we generalize our approach to study two-species reaction-cross-diffusion systems which may include nonlinearity and heterogeneity in all transport and reaction terms. We formulate our model and linearize about a steady state in Section 2. We compute general conditions for pattern formation in the spatially homogeneous version of the model in Section 2.1, and state corresponding conditions in the spatially heterogeneous case in Section 2.2. In Section 3 we solve the heterogeneous linear problem, and discuss the problem of mode selection from this solution. Using this idea, in Section 4 we derive the conditions for pattern formation in the heterogeneous case. We give a variety of numerical examples in Section 5, illustrating the utility of our theory even in cases where emergent patterns become

spatiotemporally complex. Finally we discuss a range of open mathematical problems and possible applications in Section 6.

2. Model formulation & conditions for pattern formation. As we are motivated by finding simple conditions for pattern formation, we will focus on an asymptotic regime where transport is assumed small. In [17], we related this asymptotic scale, given by ε , to diffusion coefficients, length and time scales of relevance in developmental settings, but note that such an asymptotic regime is always needed to deduce algebraic conditions for Turing conditions which are independent of the spectrum of the spatial operator; see Chapter 2 of [29] for further discussion of this ‘large domain’ approximation.

We consider the nonlinear heterogeneous cross-diffusion system,

$$\frac{\partial u}{\partial t} = \varepsilon^2 \frac{\partial}{\partial x} \left(D_{11}(u, v, x) \frac{\partial u}{\partial x} + D_{12}(u, v, x) \frac{\partial v}{\partial x} \right) + f(u, v, x), \tag{1}$$

$$\frac{\partial v}{\partial t} = \varepsilon^2 \frac{\partial}{\partial x} \left(D_{21}(u, v, x) \frac{\partial u}{\partial x} + D_{22}(u, v, x) \frac{\partial v}{\partial x} \right) + g(u, v, x), \tag{2}$$

where we have nondimensionalized the model to be in $x \in [0, 1]$, and assume sufficient regularity on the six nonlinear functions D_{ij}, f, g . We also henceforth assume $0 < \varepsilon \ll 1$, noting that in terms of a physical diffusion scale, D , a lengthscale L and timescale T , we have from model non-dimensionalization that

$$\varepsilon^2 = \frac{DT}{L^2}, \tag{3}$$

which continuously decreases as the scale of diffusion decreases for instance.

More compactly we write this system as

$$\frac{\partial \mathbf{u}}{\partial t} = \varepsilon^2 \frac{\partial}{\partial x} \left(\mathbf{D}(\mathbf{u}, x) \frac{\partial \mathbf{u}}{\partial x} \right) + \mathbf{f}(\mathbf{u}, x), \tag{4}$$

with

$$\mathbf{u} = \begin{pmatrix} u \\ v \end{pmatrix}, \mathbf{D}(\mathbf{u}, x) = \begin{pmatrix} D_{11}(u, v, x) & D_{12}(u, v, x) \\ D_{21}(u, v, x) & D_{22}(u, v, x) \end{pmatrix}, \mathbf{f}(\mathbf{u}, x) = \begin{pmatrix} f(u, v, x) \\ g(u, v, x) \end{pmatrix}. \tag{5}$$

We assume for all $\mathbf{u} \in \mathbb{R}^2$ (or in a suitably chosen subset) and $x \in [0, 1]$ that $\mathbf{D}(\mathbf{u}, x)$ is positive definite (that is, all of its eigenvalues remain positive definite). This implies that no-flux and Neumann boundary conditions are equivalent, so for concreteness we write

$$\frac{\partial u}{\partial x}(t, 0) = \frac{\partial u}{\partial x}(t, 1) = \frac{\partial v}{\partial x}(t, 0) = \frac{\partial v}{\partial x}(t, 1) = 0, \text{ for all } t \geq 0. \tag{6}$$

We let $\widehat{\mathbf{u}}^* = (u_s, v_s)^T$ be a steady state of our system, so that it satisfies

$$\mathbf{0} = \varepsilon^2 \frac{\partial}{\partial x} \left(\mathbf{D}(\widehat{\mathbf{u}}^*, x) \frac{\partial \widehat{\mathbf{u}}^*}{\partial x} \right) + \mathbf{f}(\widehat{\mathbf{u}}^*, x), \tag{7}$$

as well as the Neumann boundary conditions (6). In general, finding such a steady state analytically is extremely hard, but we can approximate it in the limit of small ε . If $\varepsilon = 0$, we have that a heterogeneous steady state would satisfy

$$\mathbf{f}(\mathbf{u}^*, x) = \mathbf{0}, \tag{8}$$

which coincides exactly with a homogeneous steady state in the case that \mathbf{u}^* does not depend on x . If we assume that such a function \mathbf{u}^* has sufficiently well-behaved derivatives, that is $|\partial \mathbf{u}^* / \partial x| = o(1/\varepsilon)$, and satisfies the boundary conditions (6),

then it is an asymptotic approximation to a solution of Eq. (7), that is $\mathbf{u}^* = \widehat{\mathbf{u}}^* + O(\varepsilon^2)$. In the following we will not distinguish between $\widehat{\mathbf{u}}^*$ satisfying Eq. (7), and \mathbf{u}^* satisfying Eq. (8), as we will only expand to order ε .

We now consider linear stability of a steady state satisfying (7), introducing another small parameter $|\delta| \ll 1$ which will be asymptotically smaller than ε . We expand our solutions as $\mathbf{u} = \mathbf{u}^*(x) + \delta \mathbf{w}(t, x)$ and substitute this into (4) to find

$$\delta \frac{\partial \mathbf{w}}{\partial t} = \varepsilon^2 \frac{\partial}{\partial x} \left(\mathbf{D}(\mathbf{u}^* + \delta \mathbf{w}, x) \left(\frac{\partial \mathbf{u}^*}{\partial x} + \delta \frac{\partial \mathbf{w}}{\partial x} \right) \right) + \mathbf{f}(\mathbf{u}^*, x) + \delta \mathbf{J}(\mathbf{u}^*, x) \mathbf{w} + O(\delta^2), \quad (9)$$

where we have expanded the kinetics \mathbf{f} in a Taylor series about δ , and hence \mathbf{J} is the Jacobian matrix evaluated at the approximate steady state. Writing \mathbf{u}_x^* as the derivative of \mathbf{u}^* with respect to x , we expand the transport term to find

$$\begin{aligned} & \frac{\partial}{\partial x} \left(\mathbf{D}(\mathbf{u}^* + \delta \mathbf{w}, x) \left(\mathbf{u}_x^* + \delta \frac{\partial \mathbf{w}}{\partial x} \right) \right) \\ &= \frac{\partial}{\partial x} (\mathbf{D}(\mathbf{u}^*, x) \mathbf{u}_x^*) + \delta \left(\mathbf{D}(\mathbf{u}^*, x) \frac{\partial^2 \mathbf{w}}{\partial x^2} + \mathbf{M} \frac{\partial \mathbf{w}}{\partial x} + \mathbf{N} \mathbf{w} \right) + O(\delta^2), \end{aligned} \quad (10)$$

where

$$\mathbf{M} = \begin{pmatrix} \frac{\partial D_{11}}{\partial x} + \frac{\partial D_{11}}{\partial u} u_x^* + \frac{\partial D_{12}}{\partial u} v_x^* & \frac{\partial D_{12}}{\partial x} + \frac{\partial D_{11}}{\partial v} u_x^* + \frac{\partial D_{12}}{\partial v} v_x^* \\ \frac{\partial D_{21}}{\partial x} + \frac{\partial D_{21}}{\partial u} u_x^* + \frac{\partial D_{22}}{\partial u} v_x^* & \frac{\partial D_{22}}{\partial x} + \frac{\partial D_{21}}{\partial v} u_x^* + \frac{\partial D_{22}}{\partial v} v_x^* \end{pmatrix}, \quad (11)$$

$$\mathbf{N} = \begin{pmatrix} \frac{\partial D_{11}}{\partial u} u_{xx}^* + \frac{\partial D_{12}}{\partial u} v_{xx}^* + \frac{\partial^2 D_{11}}{\partial u \partial x} u_x^* + \frac{\partial^2 D_{12}}{\partial u \partial x} v_x^* & \frac{\partial D_{11}}{\partial v} u_{xx}^* + \frac{\partial D_{12}}{\partial v} v_{xx}^* + \frac{\partial^2 D_{11}}{\partial v \partial x} u_x^* + \frac{\partial^2 D_{12}}{\partial v \partial x} v_x^* \\ \frac{\partial D_{21}}{\partial u} u_{xx}^* + \frac{\partial D_{22}}{\partial u} v_{xx}^* + \frac{\partial^2 D_{21}}{\partial u \partial x} u_x^* + \frac{\partial^2 D_{22}}{\partial u \partial x} v_x^* & \frac{\partial D_{21}}{\partial v} u_{xx}^* + \frac{\partial D_{22}}{\partial v} v_{xx}^* + \frac{\partial^2 D_{21}}{\partial v \partial x} u_x^* + \frac{\partial^2 D_{22}}{\partial v \partial x} v_x^* \end{pmatrix}, \quad (12)$$

and we have suppressed the dependence of $D_{ij} = D_{ij}(u^*, v^*, x)$. Throughout this paper, we will assume that \mathbf{D} , \mathbf{D}^{-1} , and \mathbf{J} have smooth and bounded coefficients, in particular with smooth and bounded derivatives with respect to x , and also with respect to u and v . Thus such properties will be inherited by \mathbf{M} and \mathbf{N} . We also remark that, as \mathbf{u}^* does not depend on ε , all of these matrices are independent of ε .

Discarding the $\text{ord}(1)$ terms¹ by using (7), and neglecting terms of $O(\delta^2)$, we obtain the linear system,

$$\frac{\partial \mathbf{w}}{\partial t} = \varepsilon^2 \left(\mathbf{D}(x) \frac{\partial^2 \mathbf{w}}{\partial x^2} + \mathbf{M}(x) \frac{\partial \mathbf{w}}{\partial x} + \mathbf{N}(x) \mathbf{w} \right) + \mathbf{J}(x) \mathbf{w}, \quad (13)$$

where we have omitted the explicit dependence on \mathbf{u}^* and its derivatives. From now on we will drop dependence on the steady state \mathbf{u}^* and view these four matrices \mathbf{D} , \mathbf{J} , \mathbf{M} and \mathbf{N} as simply depending on x . While this system appears much more complicated than that studied in [17], in fact we will show that the impact of \mathbf{M} will be confined to the structure of the unstable modes, and that both \mathbf{M} and \mathbf{N} will not have an influence on the conditions for instability and hence pattern formation. While the diffusion tensor \mathbf{D} is more general, not being confined to a diagonal matrix, its positive definiteness will be sufficient to carry out a procedure and derive results analogous to those in [17], which generalize conditions for pattern-forming instabilities to occur. Before discussing these in detail, we first review the spatially homogeneous results on such instabilities from a slightly different perspective.

¹We use the notation $\text{ord}(\varepsilon^k)$ as shorthand for ‘‘asymptotically of order k in ε .’’

2.1. Spatially Homogeneous Instability Criteria. If we assume that \mathbf{D} and \mathbf{f} do not depend on x , then (4) admits a constant steady state \mathbf{u}^* . Hence, the linearized system (13) without spatial dependencies can be written as

$$\frac{\partial \mathbf{w}}{\partial t} = \varepsilon^2 \mathbf{D} \frac{\partial^2 \mathbf{w}}{\partial x^2} + \mathbf{J} \mathbf{w}, \tag{14}$$

where the matrices \mathbf{D} and $\mathbf{J}(\mathbf{u}^*)$ are constant. We consider the usual expansion into eigenmodes of the Laplacian, $\mathbf{w} \propto e^{\lambda t} \cos(kx)$, where k takes discrete values to satisfy the boundary conditions, and hence we require k/π to be an integer for Neumann conditions. We then have that λ is an eigenvalue of $\mathbf{J} - (\varepsilon k)^2 \mathbf{D}$.

The usual way to derive instability conditions is to use the polynomial dispersion relation given by,

$$\lambda^2 - \text{tr}(\mathbf{J} - (\varepsilon k)^2 \mathbf{D}) \lambda + \det(\mathbf{J} - (\varepsilon k)^2 \mathbf{D}) = 0, \tag{15}$$

and then require $\Re(\lambda) < 0$ for $k = 0$, and $\Re(\lambda) > 0$ for some $k > 0$. The first of these entails that

$$\text{tr}(\mathbf{J}) < 0, \quad \det(\mathbf{J}) > 0, \tag{16}$$

for stability of \mathbf{u}^* in the absence of diffusion. We also have that, since \mathbf{D} is positive definite it has $\text{tr}(\mathbf{D}) > 0$ and hence by linearity of the trace we have $\text{tr}(\mathbf{J} - (\varepsilon k)^2 \mathbf{D}) = \text{tr}(\mathbf{J}) - (\varepsilon k)^2 \text{tr}(\mathbf{D}) < \text{tr}(\mathbf{J}) < 0$. For an instability for $k > 0$ we then must have a positive definite growth rate which entails, for λ real,

$$2\lambda = \text{tr}(\mathbf{J} - (\varepsilon k)^2 \mathbf{D}) + \sqrt{[\text{tr}(\mathbf{J} - (\varepsilon k)^2 \mathbf{D})]^2 - 4 \det(\mathbf{J} - (\varepsilon k)^2 \mathbf{D})} > 0. \tag{17}$$

If λ is not real, then the above implies that $\Re(\lambda) < 0$, and hence we only consider real growth rates, unless explicitly stated otherwise. The usual approach is to then maximize this growth rate as a function of k , and require $k > 0$. Instead, we will consider conditions in terms of permitted values of k to begin with, as this will generalize to the heterogeneous case as in [17].

For the marginal stability curve given by $\lambda = 0$, we see that the only remaining term of (15) implies that $(\varepsilon k)^2$ is an eigenvalue of $\mathbf{B}_0 = \mathbf{D}^{-1} \mathbf{J}$. Solving for the eigenvalues of this matrix, we then have that

$$2(\varepsilon k)^2 = \text{tr}(\mathbf{B}_0) \pm \sqrt{[\text{tr}(\mathbf{B}_0)]^2 - 4 \det(\mathbf{B}_0)} > 0, \tag{18}$$

are the two places where the graph of $\Re(\lambda(k^2))$ given by (15) crosses the k^2 -axis. For there to be a positive and real range of k^2 , we need

$$\text{tr}(\mathbf{B}_0) + \sqrt{[\text{tr}(\mathbf{B}_0)]^2 - 4 \det(\mathbf{B}_0)} > 0. \tag{19}$$

We first consider $\Re(\lambda)$ as this is always defined, real and continuous as k^2 varies. In particular for k^2 sufficiently large we have that the expression for λ in Eq. (17) gives $\Re(\lambda) < 0$. Thus if, in addition to Eq. (19), we have

$$\text{tr}(\mathbf{B}_0) - \sqrt{[\text{tr}(\mathbf{B}_0)]^2 - 4 \det(\mathbf{B}_0)} < 0, \tag{20}$$

then the graph of $\Re(\lambda(k^2))$ crosses the $k^2 \geq 0$ axis once only, with $\Re(\lambda) < 0$ for large k^2 and $\Re(\lambda)$ defined, real and continuous: this is sufficient to imply $\Re(\lambda) > 0$ as $k^2 \rightarrow 0$. In turn, this contradicts the requirement of stability at $k = 0$. Hence, for an instability range of k^2 , where $\Re(\lambda) > 0$, which does not contradict the stability requirement at $k = 0$, we require

$$\text{tr}(\mathbf{B}_0) - \sqrt{[\text{tr}(\mathbf{B}_0)]^2 - 4 \det(\mathbf{B}_0)} > 0. \tag{21}$$

Noting that $\det(\mathbf{J}) > 0 \implies \det(\mathbf{B}_0) > 0$ as \mathbf{D}^{-1} is positive definite, this then demands the conditions

$$\operatorname{tr}(\mathbf{B}_0) > 0 \text{ and } [\operatorname{tr}(\mathbf{B}_0)]^2 - 4\det(\mathbf{B}_0) > 0. \quad (22)$$

Conditions (16) and (22) are precisely the usual necessary conditions for Turing instability, which become sufficient in the limit of $\varepsilon \rightarrow 0$. We summarize these as:

Proposition 1. *Let $0 < \varepsilon \ll 1$ and assume \mathbf{J} and \mathbf{D} are constant matrices for all $x \in [0, 1]$. If we assume stability to homogeneous perturbations, i.e. the inequalities (16) are satisfied then, subject to a wave selection constraint, there exists a non-homogeneous perturbation \mathbf{w} satisfying Eq. (13) and homogeneous Neumann conditions at $x \in \{0, 1\}$ that grows exponentially in time in the interval $x \in [0, 1]$ if the inequalities (22) are satisfied.*

These are precisely the usual Turing instability conditions for the case of cross-diffusion (that is, when positive definite \mathbf{D} can be a full matrix). See [33] for general examples of such homogeneous cross-diffusion systems, with identical instability criteria given there by equations (3.15)-(3.16). Furthermore note that the wave selection constraint requires that the domain (or diffusion scale) is of a suitable size to fit a half-integer number of modes onto the domain, as required to satisfy the Neumann boundary conditions. This can always be achieved by continuously reducing the diffusion scale, D (or equivalently ε), for example, and is detailed in Murray's text [29].

2.2. Spatially heterogeneous instability criteria. In the heterogeneous case, we require stability to homogeneous perturbations across the whole domain to prevent such a mode destabilizing the system. In particular, we have the following analogous heterogeneous result:

Theorem 2.1. *Let $0 < \varepsilon \ll 1$ and assume that $[\operatorname{tr}(\mathbf{B}_0(x))]^2 - 4\det(\mathbf{B}_0(x))$ has only simple zeros for all $x \in [0, 1]$, where $\mathbf{B}_0(x) = \mathbf{D}^{-1}(x)\mathbf{J}(x)$. We assume stability to local homogeneous perturbations, i.e.*

$$\operatorname{tr}(\mathbf{J}(x)) < 0, \quad \det(\mathbf{J}(x)) > 0, \quad \text{for all } x \in [0, 1]. \quad (23)$$

Then, subject to a wave selection constraint, which can always be satisfied for a sufficiently small diffusion scale, there exists a non-homogeneous, bounded and non-trivial perturbation solution \mathbf{w} satisfying Eq. (13) and homogeneous Neumann conditions at $x \in \{0, 1\}$ that grows exponentially in time only within the interval $x \in \mathcal{T}_0$ if

$$\operatorname{tr}(\mathbf{B}_0(x)) > 0, \quad [\operatorname{tr}(\mathbf{B}_0(x))]^2 - 4\det(\mathbf{B}_0(x)) > 0, \quad \text{for all } x \in \mathcal{T}_0, \quad (24)$$

where \mathcal{T}_0 is the largest subset of $[0, 1]$ for which the conditions (24) hold.

While this statement is essentially identical to Instability Criterion 2.2 in [17], we remark that here \mathbf{D} is a full matrix and it may depend on x explicitly or via $\mathbf{u}^*(x)$. We then have that Theorem 2.1 provides a local variant for the inhomogeneous mode instability condition of Proposition 1, albeit restricted in a sense to the set $x \in \mathcal{T}_0$.

3. Asymptotic solutions of the linearized system. We proceed to develop leading ε -order WKB solutions of Eq. (13) that will be used to deduce Theorem 2.1. In Section 3.1 we first determine the leading order general WKB solution in the regime where $\varepsilon \ll 1$ and consider how to satisfy the homogeneous Neumann boundary conditions in Section 3.2, which leads to the wave selection constraint. We then

use the structure of this solution to determine the instability criteria and ultimately a deduction of Theorem 2.1 in Section 4.

3.1. WKB asymptotics. We will now find an approximate solution to Eq. (13) for small ε . As this system is linear, we can consider a solution which is separable in space and time of the form $\mathbf{w} = e^{\lambda t} \mathbf{q}(x)$. Writing \mathbf{q}' as the derivative of \mathbf{q} with respect to x , we find the problem for \mathbf{q} :

$$\mathbf{0} = \varepsilon^2 (\mathbf{D}(x)\mathbf{q}'' + \mathbf{M}(x)\mathbf{q}' + \mathbf{N}(x)\mathbf{q}) + (\mathbf{J}(x) - \lambda\mathbf{I})\mathbf{q}. \tag{25}$$

We now expand \mathbf{q} using a WKB ansatz [9, 2] in the limit of small ε as

$$\mathbf{q} = \exp\left(\frac{i\phi(x)}{\varepsilon}\right) \mathbf{p}(x), \quad \mathbf{p}(x) = \mathbf{p}_0(x) + \varepsilon\mathbf{p}_1(x) + O(\varepsilon^2). \tag{26}$$

Dropping the x dependence for notational simplicity, we compute derivatives as

$$\mathbf{q}' = \exp\left(\frac{i\phi}{\varepsilon}\right) \left(\mathbf{p}' + \frac{i\phi'}{\varepsilon}\mathbf{p}\right) = \exp\left[\frac{i\phi}{\varepsilon}\right] \frac{i\phi'}{\varepsilon}\mathbf{p}_0 + O(1), \tag{27}$$

and

$$\begin{aligned} \mathbf{q}'' &= \exp\left(\frac{i\phi}{\varepsilon}\right) \left(-\frac{\phi'^2}{\varepsilon^2}\mathbf{p} + \frac{1}{\varepsilon}(2i\phi'\mathbf{p}' + i\phi''\mathbf{p}) + \mathbf{p}''\right) \\ &= \exp\left(\frac{i\phi}{\varepsilon}\right) \left(-\frac{\phi'^2}{\varepsilon^2}\mathbf{p}_0 + \frac{1}{\varepsilon}(-\phi'^2\mathbf{p}_1 + 2i\phi'\mathbf{p}'_0 + i\phi''\mathbf{p}_0)\right) + O(1). \end{aligned} \tag{28}$$

We then have that the $O(1)$ approximation of Eq. (25) is

$$\mathbf{0} = -\phi'^2 \mathbf{D}\mathbf{p}_0 + (\mathbf{J} - \lambda\mathbf{I})\mathbf{p}_0 = \mathbf{D}[-\phi'^2 \mathbf{I} + \mathbf{B}_\lambda]\mathbf{p}_0, \tag{29}$$

where

$$\mathbf{B}_\lambda := \mathbf{D}^{-1}(\mathbf{J} - \lambda\mathbf{I})$$

and \mathbf{I} is the identity matrix. From this we see that ϕ'^2 is an eigenvalue of \mathbf{B}_λ , of which there are two (or one degenerate eigenvalue of algebraic multiplicity two), and we use $\mu_\lambda^\pm = \phi'^2_\pm$ to label the eigenvalues, which may conceivably be equal. Hence we can solve Eq. (29) by setting $\mathbf{p}_0(x) = Q_0^\pm(x)\mathbf{p}_*^\pm$ where Q_0^\pm is a scalar function and \mathbf{p}_*^\pm is the unit eigenvector associated with the eigenvalue μ_λ^\pm . Hence we can compute ϕ as the solution of

$$\phi'^2_\pm = \mu_\lambda^\pm(x) \implies \phi_\pm = C_\phi^\pm + \int_{a_\pm}^x \sqrt{\mu_\lambda^\pm(\bar{x})}d\bar{x}, \tag{30}$$

where $\mu_\lambda^\pm(x)$ denote the two eigenvalues of \mathbf{B}_λ , with C_ϕ^\pm and a_\pm constants that are to be determined. In order to compute Q_0^\pm , however, we must go to the next order in ε .

The order $O(\varepsilon)$ equation is given by

$$\begin{aligned} \mathbf{0} &= \mathbf{D}(-\phi'^2_\pm\mathbf{p}_1 + 2i\phi'_\pm\mathbf{p}'_0 + i\phi''_\pm\mathbf{p}_0) + i\phi'_\pm\mathbf{M}\mathbf{p}_0 + (\mathbf{J} - \lambda\mathbf{I})\mathbf{p}_1 \\ &= \mathbf{D}[-\phi'^2_\pm\mathbf{I} + \mathbf{B}_\lambda]\mathbf{p}_1 + 2i\phi'_\pm\mathbf{p}'_0 + i\phi''_\pm\mathbf{p}_0 + i\phi'_\pm\mathbf{D}^{-1}\mathbf{M}\mathbf{p}_0, \end{aligned} \tag{31}$$

which implies that

$$-[-\phi'^2_\pm\mathbf{I} + \mathbf{B}_\lambda]\mathbf{p}_1 = i[2\phi'_\pm Q_0^{\pm'} + \phi''_\pm Q_0^\pm + \phi'_\pm Q_0^\pm \mathbf{D}^{-1}\mathbf{M}]\mathbf{p}_*^\pm + 2i\phi'_\pm Q_0^\pm (\mathbf{p}_*^\pm)'. \tag{32}$$

The matrix premultiplying \mathbf{p}_1 has a zero eigenvalue by Eq. (29), and hence by the Fredholm Alternative Theorem we can compute a solvability condition to find Q_0^\pm and \mathbf{p}_*^\pm . Let $(\mathbf{s}_*^\pm)^T$ be the left eigenvector with zero eigenvalue and unit magnitude

of $[(-\phi_{\pm}^{\prime 2}\mathbf{I} + \mathbf{B}_{\lambda})]$. We multiply Eq. (32) on the left by $(\mathbf{s}_{*}^{\pm})^T$ to find the scalar equation

$$(2\phi'_{\pm}Q_0^{\pm} + \phi''_{\pm}Q_0^{\pm})(\mathbf{s}_{*}^{\pm})^T\mathbf{p}_{*}^{\pm} + \phi'_{\pm}Q_0^{\pm}(\mathbf{s}_{*}^{\pm})^T\mathbf{D}^{-1}\mathbf{M}\mathbf{p}_{*}^{\pm} + 2\phi'_{\pm}Q_0^{\pm}(\mathbf{s}_{*}^{\pm})^T(\mathbf{p}_{*}^{\pm})' = 0. \quad (33)$$

Solving this for Q_0^{\pm} we find

$$\frac{Q_0^{\pm}}{Q_0^{\pm}} = -\frac{\phi''_{\pm}}{2\phi'_{\pm}} - \frac{(\mathbf{s}_{*}^{\pm})^T\mathbf{D}^{-1}\mathbf{M}\mathbf{p}_{*}^{\pm} + 2(\mathbf{s}_{*}^{\pm})^T(\mathbf{p}_{*}^{\pm})'}{2(\mathbf{s}_{*}^{\pm})^T\mathbf{p}_{*}^{\pm}}, \quad (34)$$

which implies

$$Q_0^{\pm}(x) = \frac{C_Q^{\pm}}{\sqrt{\phi'_{\pm}}} \exp\left(-\int_{b_{\pm}}^x \frac{(\mathbf{s}_{*}^{\pm})^T\mathbf{D}^{-1}\mathbf{M}\mathbf{p}_{*}^{\pm} + 2(\mathbf{s}_{*}^{\pm})^T(\mathbf{p}_{*}^{\pm})'}{2(\mathbf{s}_{*}^{\pm})^T\mathbf{p}_{*}^{\pm}} d\bar{x}\right), \quad (35)$$

where C_Q^{\pm} are constants (possibly complex) and b_{\pm} are real constants. Without loss of generality, we set $b_{\pm} = a_{\pm}$ below by redefining C_Q^{\pm} .

Finally, by recasting the constants C_{ϕ} and C_Q appropriately, we can write our leading-order solution for \mathbf{w} in the trigonometric form

$$\begin{aligned} \mathbf{w}_{\pm} &= \frac{e^{\lambda t}}{(\mu_{\lambda}^{\pm}(x))^{\frac{1}{4}}} \exp\left(-\int_{a_{\pm}}^x \frac{\mathbf{s}_{*}^{\pm}(\bar{x})^T\mathbf{D}^{-1}(\bar{x})\mathbf{M}(\bar{x})\mathbf{p}_{*}^{\pm}(\bar{x}) + 2\mathbf{s}_{*}^{\pm}(\bar{x})^T\mathbf{p}_{*}^{\pm}(\bar{x})'}{2\mathbf{s}_{*}^{\pm}(\bar{x})^T\mathbf{p}_{*}^{\pm}(\bar{x})} d\bar{x}\right) \\ &\times \left[C_0^{\pm} \cos\left(\frac{1}{\varepsilon} \int_{a_{\pm}}^x \sqrt{\mu_{\lambda}^{\pm}(\bar{x})} d\bar{x}\right) + S_0^{\pm} \sin\left(\frac{1}{\varepsilon} \int_{a_{\pm}}^x \sqrt{\mu_{\lambda}^{\pm}(\bar{x})} d\bar{x}\right) \right] \mathbf{p}_{*}^{\pm}(x), \end{aligned} \quad (36)$$

where C_0^{\pm} , S_0^{\pm} are real constants. The constants a_{\pm} are not independent degrees of freedom as shifts in these constants can be accommodated by changes in C_0^{\pm} , S_0^{\pm} but it will be convenient to keep the above form for \mathbf{w}_{\pm} . Furthermore, for fixed λ , the solution \mathbf{w}_{\pm} given by Eq. (36) gives two modes which satisfy Eq. (13) at leading order in ε , corresponding to the two eigenvalues of \mathbf{B}_{λ} given by μ_{λ}^{+} and μ_{λ}^{-} . We remark that this solution is nearly identical to the leading-order WKB solution in [17], except for two notable differences. Firstly, there is an additional term involving the matrix \mathbf{M} here, though this will not influence the conditions we find to ensure we have an instability, i.e. a mode with $\Re(\lambda) > 0$, given in Theorem 2.1. Secondly, the matrix \mathbf{D} is no longer diagonal, though it is still positive definite. One technical point concerns the impact of \mathbf{M} and especially \mathbf{D} on the structure of \mathbf{w}_{\pm} near singularities, as will be discussed below and which is ultimately different from the analysis presented in [17].

3.2. Admissible growth rates. The special case of $\mathbf{D} = \text{diag}(1, d)$, $\mathbf{M} = \mathbf{N} = \mathbf{0}$ has previously been considered in [17], with a proof of the analogue of Theorem 2.1 that is generalised to cross-diffusion below, together with a highlighting of where the differences are. As in [17], our starting point is Eq. (36) and when such WKB solutions are associated with an instability that drives the system away from its steady state. That is, we look for WKB modes given by Eq. (36) which approximate a solution of Eq. (13) with $\Re(\lambda) > 0$.

Our first consideration, directly analogous to [17], is whether the WKB solution is defined for all $x \in [0, 1]$. If so, leading order Neumann boundary conditions at $\{0, 1\}$ entail

$$\int_0^1 \sqrt{\mu_{\lambda}^{\pm}(\bar{x})} d\bar{x} = \frac{1}{2} n\pi\varepsilon, \quad (37)$$

where, without loss of generality, n is a positive integer and $a_{\pm} = S_0^{\pm} = 0$, yielding a WKB cosine solution. Further, given a suitable choice of a sufficiently small ε , the constraint given by Eq. (37) can be ensured simply by imposing

$$\int_0^1 \sqrt{\mu_{\lambda}^{\pm}(\bar{x})} d\bar{x} \in \mathbb{R}^+, \tag{38}$$

where \mathbb{R}^+ denotes the positive reals and thus the square root in the integrand is the positive square root. The distinction between the two cases, in particular where the more general case Eq. (38) holds, but Eq. (37) does not, is equivalent to the wave selection constraint in the standard Turing instability, which is a well-understood constraint that is additional to the canonical Turing instability conditions of Eqs. (16), (22) [29].

However, a non-trivial WKB solution (36) need not be defined everywhere on the domain $x \in [0, 1]$. More generally, the steady state may be destabilized by WKB solutions that are only non-zero on one or more intervals of the form (a, b) with $0 \leq a < b \leq 1$. As will be investigated below, this will occur due to terms contributing to w_{\pm} in Eq. (36) becoming unbounded on approaching an interior point, say $x = a$. We therefore introduce ‘internal’ boundary conditions at such points which allow us to match a non-zero WKB mode on an interval (a, b) , which we match to a zero solution outside of this interval. Thus, as demonstrated below, an internal homogeneous Dirichlet boundary condition $w_{\pm}(a) = \mathbf{0}$ with $a_{\pm} = a$ in Eq. (36) is then necessary and sufficient for a well-defined solution local to $x = a$. We may accommodate both cases – homogeneous Neumann or internal Dirichlet boundary conditions – by requiring

$$\int_a^b \sqrt{\mu_{\lambda}^{\pm}(\bar{x})} d\bar{x} \in \mathbb{R}^+ \tag{39}$$

for a positive square root and $0 \leq a < b \leq 1$, so that the homogeneous boundary condition at $x = a, b$, whether it be Neumann or Dirichlet, can be satisfied. In particular, this requires (i) an appropriate choice of the cosine or sine solution, according to whether, respectively, a Neumann or Dirichlet condition is required at $x = a = a_{\pm}$ for the WKB solution of Eq. (36) and (ii) Eq. (39), which allows the enforcement of the boundary condition at $x = b$ for suitably small ε , with the constraint of ε constituting the wave selection constraint.

Thus for a given non-trivial interval (a, b) , Eq. (39) constitutes the fundamental condition for an unstable WKB mode to destabilize the steady state, assuming there is stability to homogeneous perturbations. Consequently, our aim below is to use Eq. (39) to deduce Theorem 2.1, including a characterization of the location of the instability regions, that is the intervals of the form (a, b) in the above discussion, whose union constitutes the set \mathcal{T}_0 in the statement of Theorem 2.1.

4. Derivation of Theorem 2.1. Extensive elements of the reasoning below are straightforward generalizations of [17], once expressions that involve the components of \mathbf{D} are rewritten in terms of $\text{tr}(\mathbf{D})$ and $\det(\mathbf{D})$, which are both positive since \mathbf{D} is positive definite. However, a new technical result (given in Proposition 7) is now required to handle a degenerate case arising at singular points, which can be very quickly dismissed for the simpler systems of [17] in contrast to the more general system considered here. In turn this alters the details of some of the derivations (given in Propositions 6, 8 and 10). We also present the propositions in a different

order to [17], with some alternative approaches, in a pedagogic attempt to simplify the derivation to aid understanding.

4.1. Relating the constraint to conditions on \mathbf{D} , \mathbf{J} and λ . As in [17], we first define *permissible* growth rates and eigenvalues which satisfy (39).

Definition 4.1. A permissible pair $(\lambda, \mu_\lambda^\pm(x))$ is a tuple such that the value of λ entails $\mu_\lambda^\pm(x)$ satisfies constraint (39) for all x in some non-empty interval $(a, b) \subseteq (0, 1)$.

We will denote λ as permissible, or $\mu_\lambda^\pm(x)$ as permissible, if $(\lambda, \mu_\lambda^\pm(x))$ is permissible, as defined above.

Proposition 2. $\mu_\lambda^\pm(x)$ is permissible if and only if $\mu_\lambda^\pm(x)$ is real and non-negative for all $x \in (a, b)$, though not identically zero.

Proof. If $\mu_\lambda^\pm(x)$ is real, non-negative and not identically zero for $x \in (a, b)$ then it is immediately clear that it is permissible. Conversely, let $\mu_\lambda^\pm(x)$ be permissible. Given the square root in condition (39) is the positive one, and working in the complex plane such that any argument, denoted θ below, is in the range $\theta \in [0, 2\pi)$ then the square root of $z = r \exp(i\theta)$, $r \geq 0$, is given by $\sqrt{r}e^{i\theta/2}$. Hence, any imaginary contribution to $\sqrt{\mu_\lambda^\pm(x)}$, in condition (39) is non-negative as $\theta/2 \in [0, \pi)$ and cannot be cancelled from elsewhere in the integration domain. Thus, given Eq. (39), $\sqrt{\mu_\lambda^\pm(x)}$ must be real for all $x \in (a, b)$. Hence, $\mu_\lambda^\pm(x)$ is real and non-negative for all $x \in (a, b)$, while $\mu_\lambda^\pm(x)$ cannot be identically zero as the integral in Eq. (39) is not zero. \square

Proposition 3. Assume λ is permissible for $x \in (a, b)$. If λ has a non-zero imaginary part, $\Im(\lambda) \neq 0$, then $\Re(\lambda) < 0$ for $x \in (a, b)$. Equivalently, if $\Re(\lambda) \geq 0$ then $\Im(\lambda) = 0$ for $x \in (a, b)$.

Proof. From the definition of $\mu_\lambda^\pm(x)$, we have

$$\det[-\mu_\lambda^\pm(x)\mathbf{D} + \mathbf{J}_\lambda(x)] = \det[-\mu_\lambda^\pm(x)\mathbf{D} + \mathbf{J} - \lambda\mathbf{I}] = 0, \quad (40)$$

and so, dropping the explicit x -dependence,

$$2\lambda = \operatorname{tr}(-\mu_\lambda^\pm\mathbf{D} + \mathbf{J}) \pm \sqrt{[\operatorname{tr}(-\mu_\lambda^\pm\mathbf{D} + \mathbf{J})]^2 - 4 \det[-\mu_\lambda^\pm(x)\mathbf{D} + \mathbf{J}]}, \quad (41)$$

with the spatial dependence of $\mu_\lambda^\pm(x)$ such that the growth rate, λ , does not have a dependence on x . We have $\operatorname{tr}(\mathbf{J}) < 0$ for all x by Eq. (23) and, given λ is permissible for $x \in (a, b)$, so that $\mu_\lambda^\pm(x)$ is permissible on this region, $\operatorname{tr}(-\mu_\lambda^\pm(x)\mathbf{D}) < 0$ for $x \in (a, b)$. Thus, if a permissible λ is complex, then it must have a negative real part. \square

Proposition 4. Given $(\lambda, \mu_\lambda^\pm(x))$ is permissible for $x \in (a, b)$ and $\Re(\lambda) \geq 0$, then $\det(\mathbf{B}_\lambda) > 0$, where $\mathbf{B}_\lambda = \mathbf{D}^{-1}(\mathbf{J} - \lambda\mathbf{I}) = \mathbf{D}^{-1}\mathbf{J}_\lambda$.

Proof. We have that λ is real by Proposition 3 and is thus non-negative, with

$$\det(\mathbf{B}_\lambda) = \det(\mathbf{D}^{-1}) \det(\mathbf{J}_\lambda) = \det(\mathbf{D}^{-1}) (\lambda^2 - \lambda \operatorname{tr}(\mathbf{J}) + \det(\mathbf{J})) > 0$$

for all $x \in (a, b)$, where the final inequality arises from the positive definiteness of \mathbf{D} , and Eq. (23). \square

Proposition 5. *Given $\Re(\lambda) \geq 0$, the pair $(\lambda, \mu_\lambda^\pm(x))$ is permissible on $x \in (a, b)$ if and only if*

$$\text{tr}(\mathbf{B}_\lambda) > 0, \quad [\text{tr}(\mathbf{B}_\lambda)]^2 - 4 \det(\mathbf{B}_\lambda) \geq 0, \tag{42}$$

for $x \in (a, b)$.

Proof. We immediately have

$$\mu_\lambda^\pm(x) = \frac{1}{2} \left[\text{tr}(\mathbf{B}_\lambda) \pm \sqrt{[\text{tr}(\mathbf{B}_\lambda)]^2 - 4 \det(\mathbf{B}_\lambda)} \right] \tag{43}$$

since μ_λ^\pm are defined to be the eigenvalues of \mathbf{B}_λ . Given conditions (42), we can see by Equation (43) that $\mu_\lambda^\pm(x) > 0$ for all $x \in (a, b)$, and, hence, condition (39) is satisfied, giving permissibility.

Next we consider the converse by assuming $(\lambda, \mu_\lambda^\pm(x))$ is permissible for $x \in (a, b)$. Then $\Re(\lambda) \geq 0$ implies λ is real by Proposition 3. From permissibility and Proposition 2 we also have that $\mu_\lambda^\pm(x)$ is real, non-negative and not identically zero for $x \in (a, b)$. As $\mu_\lambda^\pm(x)$ and λ are real, this enforces

$$[\text{tr}(\mathbf{B}_\lambda)]^2 - 4 \det(\mathbf{B}_\lambda) \geq 0$$

for $x \in (a, b)$. Also $\det(\mathbf{B}_\lambda) > 0$ on this region by Proposition 4 and hence for both the positive and negative square root in Equation (43), the fact that $\mu_\lambda^\pm(x)$ cannot be negative enforces $\text{tr}(\mathbf{B}_\lambda) \geq 0$ for $x \in (a, b)$. The possibility that $\text{tr}(\mathbf{B}_\lambda) = 0$ is excluded as then $\mu_\lambda^\pm(x)$ is not real, since $\det(\mathbf{B}_\lambda) > 0$. \square

Note that the conditions in Proposition 5 translate the constraint (39) from the WKB solutions, \mathbf{w}_\pm of Eq. (36), to properties of \mathbf{B}_λ and thus properties of \mathbf{J} , \mathbf{D} and λ . Furthermore the conditions in Proposition 5 do not depend on the positive or negative branch of μ_λ^\pm , implying that both eigenvalues are permissible given that one of them is.

4.2. Prospective blow-up and regularization of WKB solutions. *A priori*, there is scope for the WKB solutions, \mathbf{w}_\pm of Eq. (36), to become unbounded, either within the region of permissibility (a, b) , or at its edges, $\{a, b\}$ due to a zero of the denominator of $2\mathbf{s}_{*\pm}^T \mathbf{p}_{*\pm}$ within the integrand of the exponent or at the edges due to denominator $(\mu_\lambda^\pm)^{1/4}$.

However, Propositions 4, 5 show that given $(\lambda, \mu_\lambda^\pm(x))$ is permissible and $\Re(\lambda) \geq 0$ on $x \in (a, b)$ the eigenvalues μ_λ^\pm , as given by

$$\mu_\lambda^\pm(x) = \frac{1}{2} \left[\text{tr}(\mathbf{B}_\lambda) \pm \sqrt{[\text{tr}(\mathbf{B}_\lambda)]^2 - 4 \det(\mathbf{B}_\lambda)} \right], \tag{44}$$

are bounded away from zero on $x \in (a, b)$. Thus the denominator $(\mu_\lambda^\pm)^{1/4}$ is bounded away from zero on (a, b) and thus cannot generate blow-up in the WKB solutions on approaching either of the points $\{a, b\}$.

However, there is still scope for the denominator of $2\mathbf{s}_{*\pm}^T \mathbf{p}_{*\pm}$ within the integrand of the exponent to generate blow-up. Thus we first determine conditions on \mathbf{B}_λ for such a blow-up to occur and proceed to demonstrate that it can be regularized, i.e. bounded, on use of an internal homogeneous Dirichlet boundary condition where the WKB solution would otherwise blow-up. The resulting non-trivial WKB solution will match a trivial zero solution exterior to the region of permissibility (if the prospective blow-up location is not on the edge of the domain $[0, 1]$.) Below, for notational convenience and brevity, we drop the \pm labels on $(\mathbf{s}_*^\pm)^T$ and \mathbf{p}_*^\pm .

Proposition 6. *Given $(\lambda, \mu_\lambda^\pm(x))$ is permissible and $\Re(\lambda) \geq 0$ for $x \in (a, b)$, then*

$$[\operatorname{tr}(\mathbf{B}_\lambda)]^2 - 4 \det(\mathbf{B}_\lambda) > 0$$

for $x \in (a, b)$ if and only if $\mathbf{s}_*^T \mathbf{p}_* \neq 0$ for all $x \in (a, b)$, where \mathbf{s}_* and \mathbf{p}_* are the left and right unit eigenvectors of $[-\mu_\lambda^\pm \mathbf{I} + \mathbf{B}_\lambda]$.

Proof. We will demonstrate both implications via contraposition. We first assume that $\mathbf{s}_*^T \mathbf{p}_* = 0$ at some point $x_* \in (a, b)$. By elaborating possibilities on a case by case basis for a general 2×2 matrix with zero determinant, we note that the left and right eigenvectors of the zero eigenvalue can only be perpendicular if the matrix is proportional to one of the following:

$$\begin{pmatrix} 0 & 0 \\ 0 & 0 \end{pmatrix}, \begin{pmatrix} 1 & 1 \\ -1 & -1 \end{pmatrix}, \begin{pmatrix} 1 & -1 \\ 1 & -1 \end{pmatrix}.$$

In all three cases, we have that the trace is zero. Therefore,

$$\operatorname{tr}(-\mu_\lambda^\pm \mathbf{I} + \mathbf{B}_\lambda) = -2\mu_\lambda^\pm + \operatorname{tr}(\mathbf{B}_\lambda) = 0.$$

However, by Eq. (43), this implies that $[\operatorname{tr}(\mathbf{B}_\lambda)]^2 - 4 \det(\mathbf{B}_\lambda) = 0$, contradicting the assumption that this quantity remains positive.

For the converse, we start from $[\operatorname{tr}(\mathbf{B}_\lambda)]^2 - 4 \det(\mathbf{B}_\lambda) = 0$ at some point $x_* \in (a, b)$ (noting that if this term were negative, then, by Proposition 5, λ would not be permissible and we would have an immediate contradiction). By using Equation (43) again we see that $\operatorname{tr}(-\mu_\lambda^\pm \mathbf{I} + \mathbf{B}_\lambda) = 0$, while $\det(-\mu_\lambda^\pm \mathbf{I} + \mathbf{B}_\lambda) = 0$ as μ_λ^\pm are the eigenvalues of \mathbf{B}_λ . Any real 2×2 matrix with zero determinant and trace can be written in one of the following forms:

$$\begin{pmatrix} c_1 & c_2 \\ -\frac{c_1^2}{c_2} & -c_1 \end{pmatrix}, \begin{pmatrix} 0 & 0 \\ c_2 & 0 \end{pmatrix}, \begin{pmatrix} 0 & c_2 \\ 0 & 0 \end{pmatrix}, \begin{pmatrix} 0 & 0 \\ 0 & 0 \end{pmatrix}, \quad (45)$$

for real $c_1 \neq 0$ and real $c_2 \neq 0$. The first of these has one left and one right eigenvector given, respectively, by $\mathbf{s}_*^T = (c_1, c_2)$ and $\mathbf{p}_*^T = (-c_2, c_1)$, to within normalization and which satisfy $\mathbf{s}_*^T \mathbf{p}_* = 0$. For the second matrix case, we have $\mathbf{p}_*^T = (0, 1)$ and $\mathbf{s}_*^T = (1, 0)$ which are also orthogonal, and similarly for the third case with $\mathbf{p}_*^T = (1, 0)$ and $\mathbf{s}_*^T = (0, 1)$.

The final case is not possible given the constraints on the system. Specifically, we have that $\mathbf{J} - \lambda \mathbf{I} = \mathbf{D} \mathbf{B}_\lambda = \mu_\lambda^\pm \mathbf{D}$, where we note that the constraint that μ_λ^\pm being permissible implies that μ_λ^\pm is real and non-negative by Proposition 2, and we have the restriction $\Re(\lambda) \geq 0$. Hence taking the trace of $\mathbf{J} = \lambda \mathbf{I} + \mu_\lambda^\pm \mathbf{D}$ we have

$$\operatorname{tr}(\mathbf{J}) = 2\lambda + \mu_\lambda^\pm \operatorname{tr}(\mathbf{D}) \geq 0,$$

where we have used the fact that \mathbf{D} is positive definite. The above inequality contradicts the requirement of stability to homogeneous perturbations, Eq. (23). \square

We proceed to consider whether there is a singularity when

$$\mathbf{s}_*^T \mathbf{p}_* = 0 = [\operatorname{tr}(\mathbf{B}_\lambda)]^2 - 4 \det(\mathbf{B}_\lambda)$$

subject to weak constraints on the nature of the zero, which are given via the definition of an *Admissible Neighborhood* immediately below.

Definition 4.2. Admissible Neighborhood. Let $(\lambda, \mu_\lambda^\pm(x))$ be permissible for $x \in (a, b)$ and $\Re(\lambda) \geq 0$, with a simple zero of

$$[\operatorname{tr}(\mathbf{B}_\lambda)]^2 - 4 \det(\mathbf{B}_\lambda) = 0$$

at a point $X_* \in \{a, b\}$. We can then write

$$[\text{tr}(\mathbf{B}_\lambda)]^2 - 4 \det(\mathbf{B}_\lambda) = A^2|x - X_*|(1 + o(1)), \quad x \in \mathcal{N}$$

where $A > 0$ without loss, given the *admissible neighborhood* \mathcal{N} is defined as follows. If $X_* = a$ then,

$$[\text{tr}(\mathbf{B}_\lambda)]^2 - 4 \det(\mathbf{B}_\lambda) > 0$$

to the right of X_* and \mathcal{N} is the closure of the intersection of a sufficiently small, non-empty neighborhood of X_* with the set $x \geq X_* = a$. In particular, the neighborhood is sufficiently small to ensure no other zero of $[\text{tr}(\mathbf{B}_\lambda)]^2 - 4 \det(\mathbf{B}_\lambda)$ is within $\mathcal{N}/\{X_*\}$. If $X_* = b$, then \mathcal{N} is an analogously defined closure of a half-neighborhood contained within $[a, b]$.

In particular we need to consider how the solution behaves sufficiently close to a simple zero. To proceed we first need to determine the behavior of $-\mu_\lambda^\pm \mathbf{I} + \mathbf{B}_\lambda$ sufficiently close to a simple zero, as summarized by the following proposition.

Proposition 7. *Let $(\lambda, \mu_\lambda^\pm(x))$ be permissible and $\Re(\lambda) \geq 0$ for $x \in (a, b)$. Suppose that a point $X_* \in \{a, b\}$ is a simple zero of $[\text{tr}(\mathbf{B}_\lambda)]^2 - 4 \det(\mathbf{B}_\lambda)$, with associated admissible neighborhood \mathcal{N} , as in Definition 4.2. Then for x in \mathcal{N} excluding the singularity point, that is $x \in \mathcal{N}/\{X_*\}$, we have*

$$-\mu_\lambda^\pm \mathbf{I} + \mathbf{B}_\lambda = \begin{pmatrix} c_1(x) & c_2(x) \\ \frac{c_1(x)}{c_2(x)}(-c_1(x) + K(x)) & -c_1(x) + K(x) \end{pmatrix}, \quad (46)$$

where

$$K(x) = \text{tr}(-\mu_\lambda^\pm \mathbf{I} + \mathbf{B}_\lambda) = \mp A|x - X_*|^{1/2}(1 + o(1)), \quad A > 0,$$

with the \mp inherited from the \pm of μ_λ^\pm and $c_2(x)$ is non-zero for $x \in \mathcal{N}$, with restrictions on \mathcal{N} as required.

Proof. We first of all note that from Eq. (44) and Definition 4.2,

$$K(x) := \text{tr}(-\mu_\lambda^\pm \mathbf{I} + \mathbf{B}_\lambda) = \mp A|x - X_*|^{1/2}(1 + o(1)), \quad (47)$$

where $A > 0$. Noting that

$$\det(-\mu_\lambda^\pm \mathbf{I} + \mathbf{B}_\lambda) = 0, \quad x \in \mathcal{N}$$

then, with the zero determinant constraint $\alpha(x)(K(x) - \alpha(x)) = \beta(x)\gamma(x)$, we can write, without loss of generality, that

$$-\mu_\lambda^\pm \mathbf{I} + \mathbf{B}_\lambda = \begin{pmatrix} \alpha(x) & \beta(x) \\ \gamma(x) & K(x) - \alpha(x) \end{pmatrix}. \quad (48)$$

If $\beta(X_*) \neq 0$, then restricting \mathcal{N} as necessary, we have $\beta(x) \neq 0$ for $x \in \mathcal{N}$. In this case we can write

$$-\mu_\lambda^\pm \mathbf{I} + \mathbf{B}_\lambda = \begin{pmatrix} c_1(x) & c_2(x) \\ \frac{c_1(x)}{c_2(x)}(-c_1(x) + K(x)) & -c_1(x) + K(x) \end{pmatrix}, \quad (49)$$

where $c_2(x)$ is non-zero for $x \in \mathcal{N}$. Hence the proposition holds if $\beta(X_*) \neq 0$.

We now consider the degeneracy with $\beta(X_*) = 0$, which implies $\alpha(X_*) = 0$ on noting that $K(X_*) = 0$. From Eq. (48) and Eq. (44), together with the smoothness

of \mathbf{B}_λ allowing its expansion about $x = x_*$, we have

$$\begin{aligned} \alpha(x) &= -\mu_\lambda^\pm + (\mathbf{B}_\lambda)_{11}(x) \\ &= \frac{1}{2}((\mathbf{B}_\lambda)_{11}(X_*) - (\mathbf{B}_\lambda)_{22}(X_*)) \mp \frac{1}{2}A|x - X_*|^{1/2}(1 + o(1)) + O(|x - X_*|) \end{aligned}$$

and $\alpha(X_*) = 0$ implies $(\mathbf{B}_\lambda)_{11}(X_*) = (\mathbf{B}_\lambda)_{22}(X_*)$. Hence, noting that any $O(|x - X_*|)$ terms can be absorbed into the $|x - X_*|^{1/2}o(1)$ terms, we have

$$K(x) - \alpha(x) = \mp \frac{1}{2}A|x - X_*|^{1/2}(1 + o(1)),$$

and thus

$$\beta(x)\gamma(x) = \alpha(x)(K(x) - \alpha(x)) = \frac{1}{4}A^2|x - X_*|(1 + o(1)).$$

Hence for $x \in \mathcal{N}/\{X_*\}$, restricting \mathcal{N} as necessary to ensure the validity of the above local expansions, we have $\beta(x) \neq 0$. Hence for $x \in \mathcal{N}/\{X_*\}$, Eq. (46) applies, demonstrating the proposition for $\beta(X_*) = 0$. \square

The following propositions proceed to consider how

$$\exp\left(\int \frac{\mathbf{s}_*(\bar{x})^T \mathbf{D}^{-1}(\bar{x}) \mathbf{M}(\bar{x}) \mathbf{p}_*(\bar{x}) + 2\mathbf{s}_*(\bar{x})^T \mathbf{p}'_*(\bar{x})}{2\mathbf{s}_*(\bar{x}) \cdot \mathbf{p}_*(\bar{x})} d\bar{x}\right)$$

behaves for appropriate integration limits sufficiently close to the simple zero X_* , before returning to considering the WKB solution of Eq. (36).

Proposition 8. *Let $(\lambda, \mu_\lambda^\pm(x))$ be permissible and $\Re(\lambda) \geq 0$ for $x \in (a, b)$. Suppose that a point $X_* \in \{a, b\}$ is a simple zero of $[\text{tr}(\mathbf{B}_\lambda)]^2 - 4\det(\mathbf{B}_\lambda)$, with associated admissible neighborhood \mathcal{N} , as in Definition 4.2. Then, if $X_* = a$, and with $x \in \mathcal{N}$, $x > X_* = a$, we have*

$$\exp\left(\int_{X_*+\eta}^x \frac{\mathbf{s}_*(\bar{x})^T \mathbf{D}^{-1}(\bar{x}) \mathbf{M}(\bar{x}) \mathbf{p}_*(\bar{x}) + 2\mathbf{s}_*(\bar{x})^T \mathbf{p}'_*(\bar{x})}{2\mathbf{s}_*(\bar{x}) \cdot \mathbf{p}_*(\bar{x})} d\bar{x}\right) = \text{ord}\left(\frac{1}{\eta^{1/4}}\right), \tag{50}$$

as $\eta \rightarrow 0^+$. If instead $X_* = b$ with $x \in \mathcal{N}$, i.e. $x < X_* = b$, we have (noting the sign difference in the exponent)

$$\exp\left(-\int_x^{X_*-\eta} \frac{\mathbf{s}_*(\bar{x})^T \mathbf{D}^{-1}(\bar{x}) \mathbf{M}(\bar{x}) \mathbf{p}_*(\bar{x}) + 2\mathbf{s}_*(\bar{x})^T \mathbf{p}'_*(\bar{x})}{2\mathbf{s}_*(\bar{x}) \cdot \mathbf{p}_*(\bar{x})} d\bar{x}\right) = \text{ord}\left(\frac{1}{\eta^{1/4}}\right), \tag{51}$$

as $\eta \rightarrow 0^+$.

Proof. By Proposition 7 we have

$$\begin{aligned} & -\mu_\lambda^\pm \mathbf{I} + \mathbf{B}_\lambda \\ &= \begin{pmatrix} c_1(x) & c_2(x) \\ \frac{c_1(x)}{c_2(x)} \left(-c_1(x) \mp A|x - X_*|^{1/2}(1 + o(1))\right) & -c_1(x) \mp A|x - X_*|^{1/2}(1 + o(1)) \end{pmatrix}, \end{aligned} \tag{52}$$

for $x \in \mathcal{N}/\{X_*\}$, where $c_2(x) \neq 0$.

Noting overall sign choices are without loss of generality due to the parity of the integrands in Eqs. (50), (51), we have that the unit right zero eigenvector of the matrix (52) can be written as

$$\mathbf{p}_* = \frac{1}{N_1} \begin{pmatrix} -c_2 \\ c_1 \end{pmatrix}, \quad N_1 = (c_1^2 + c_2^2)^{1/2} \geq |c_2(x)| > 0,$$

where N_1 is a normalization factor. Similarly the left unit eigenvector of matrix (52) is

$$\mathbf{s}_*^T = \frac{1}{N_2} \left(\frac{1}{c_2} \left(c_1 \pm A|x - X_*|^{1/2}(1 + o(1)) \right), 1 \right),$$

where $N_2 \geq 1$ is a normalization factor.

Further, from the first row of Eq. (52), we have

$$c_1(x) = (\mathbf{B}_\lambda)_{11} - \frac{1}{2}\text{tr}(\mathbf{B}_\lambda)(X_*) \mp \frac{A}{2}|x - X_*|^{1/2}(1 + o(1)), \quad c_2(x) = (\mathbf{B}_\lambda)_{12},$$

where $(\mathbf{B}_\lambda)_{11}, (\mathbf{B}_\lambda)_{12}$ are components of \mathbf{B}_λ and thus smooth under differentiation with respect to x . Thus $c_2'(x)$ is bounded on $x \in \mathcal{N}/\{X_*\}$, while

$$c_1'(x) = \mp \frac{A}{4}\sigma_{X_*}|x - X_*|^{-1/2}(1 + o(1)), \quad \sigma_{X_*} := \begin{cases} 1 & X_* = a \\ -1 & X_* = b \end{cases}.$$

To determine a leading order approximation for \mathbf{p}'_* , the derivative of \mathbf{p}_* , note that $c_1'(x)$ will have a large derivative in \mathcal{N} , giving

$$\mathbf{p}'_* = \frac{1}{N_1} \begin{pmatrix} 0 \\ \mp \frac{A}{4}\sigma_{X_*}|x - X_*|^{-1/2} \end{pmatrix} (1 + o(1)),$$

as all other derivatives are $\text{ord}(1)$, except for the derivative of c_1 in the denominator, that is N_1 . As this is in the denominator however, it will suppress, rather than elevate, the asymptotic order of the resulting term. Further note that $\mathbf{s}_*(\bar{x}), \mathbf{p}_*(\bar{x})$ are normalized by construction and thus have components that are $O(1)$ on approaching the singular point. Similarly, from our assumptions that $\mathbf{D}, \mathbf{D}^{-1}$ and \mathbf{J} have smooth and bounded coefficients we also have $\mathbf{M}(\bar{x})$ has bounded coefficients, that is, the coefficients are $O(1)$ on approaching the simple zero, X_* . Hence we have

$$\mathbf{s}_*(\bar{x})^T \mathbf{D}^{-1}(\bar{x}) \mathbf{M}(\bar{x}) \mathbf{p}_*(\bar{x}) \sim O(1)$$

and thus

$$\begin{aligned} \frac{\mathbf{s}_*(\bar{x})^T \mathbf{D}^{-1}(\bar{x}) \mathbf{M}(\bar{x}) \mathbf{p}_*(\bar{x}) + 2\mathbf{s}_*(\bar{x})^T \mathbf{p}'_*(\bar{x})}{2\mathbf{s}_*(\bar{x}) \cdot \mathbf{p}_*(\bar{x})} &= \frac{\mathbf{s}_*(\bar{x})^T \mathbf{p}'_*(\bar{x})}{\mathbf{s}_*(\bar{x}) \cdot \mathbf{p}_*(\bar{x})} (1 + o(1)) \\ &= \frac{1}{4}\sigma_{X_*} \frac{1}{|x - X_*|} (1 + o(1)) \end{aligned}$$

for $x \in \mathcal{N}/\{X_*\}$ since the dominant contribution in the numerator of the latter relation is from the singularity term scaling with $|x - X_*|^{-1/2}$ within \mathbf{p}'_* , noting that this vector is *not* normalized.

Hence, fixing $\eta > 0$ sufficiently small, with $X_* = a, x \geq X_* + \eta, x \in \mathcal{N}/\{X_*\}$ we have that the left-hand side of Eq. (50) reduces to

$$\exp \left(\int_{X_* + \eta}^x \frac{1}{4(\bar{x} - X_*)} (1 + o(1)) d\bar{x} \right) \sim \text{ord} \left(\frac{1}{\eta^{1/4}} \right), \tag{53}$$

providing the required result on subsequently considering $\eta \rightarrow 0^+$. Analogously, for sufficiently small, fixed, $\eta > 0$ with $X_* = b, x \leq X_* - \eta, x \in \mathcal{N}/\{X_*\}$ we have the left-hand side of Eq. (51) reduces to

$$\exp \left(\int_x^{X_* - \eta} \frac{1}{4(X_* - \bar{x})} (1 + o(1)) d\bar{x} \right) \sim \text{ord} \left(\frac{1}{\eta^{1/4}} \right), \tag{54}$$

giving the required result on now taking the limit $\eta \rightarrow 0^+$. □

We can use the results of the above proposition to demonstrate that the behavior of the WKB solution is singular as $[\text{tr}(\mathbf{B}_\lambda)]^2 - 4 \det(\mathbf{B}_\lambda)$ approaches zero from above, but that the singularity can be regularized with an appropriate Dirichlet boundary condition. Firstly, note the WKB solutions are only defined up to a multiplicative scaling so that on a region (a, b) with $0 \leq a < b \leq 1$, we need to assign an overall scale, which we impose at the center of the domain $X_{**} = (a + b)/2$ by setting

$$Q_0^\pm(X_{**}) = \text{ord}(1).$$

Thus for $\eta > 0$ sufficiently small we are interested in the behavior of Q_0 , normalized by its value at X_{**} as this will dictate the behavior of \mathbf{w}_\pm , as we now characterize in the following proposition.

Proposition 9. *Let $(\lambda, \mu_\lambda^\pm(x))$ be permissible and $\Re(\lambda) \geq 0$ for $x \in (a, b)$. Suppose that a point $X_* \in \{a, b\}$ is a simple zero of $[\text{tr}(\mathbf{B}_\lambda)]^2 - 4 \det(\mathbf{B}_\lambda)$, with associated admissible neighborhood \mathcal{N} , as in Definition 4.2. Defining $X_{**} := (a+b)/2$, $\sigma_{X_*} = 1$ if $X_* = a$ and $\sigma_{X_*} = -1$ if $X_* = b$ we have*

$$\frac{Q_0^\pm(X_* + \sigma_{X_*}\eta)}{Q_0^\pm(X_{**})} \sim \text{ord}\left(\frac{1}{\eta^{1/4}}\right)$$

on $x \in \mathcal{N}/\{X_*\}$ as $\eta \rightarrow 0^+$, so that from Eq. (36)

$$\mathbf{w}_\pm(X_* + \sigma_{X_*}\eta) = \text{ord}(\eta^{3/4})$$

on $x \in \mathcal{N}/\{X_*\}$ as $\eta \rightarrow 0^+$, providing homogeneous Dirichlet conditions are imposed at $x = X_*$.

Proof. Let $X_{**} = (a + b)/2$, fix $Q_0^\pm(X_{**}) = \text{ord}(1)$ for the overall scaling of the WKB solution and, for convenience, define

$$I(\bar{x}) := \frac{\mathbf{s}_*(\bar{x})^T \mathbf{D}^{-1}(\bar{x}) \mathbf{M}(\bar{x}) \mathbf{p}_*(\bar{x}) + 2\mathbf{s}_*(\bar{x})^T \mathbf{p}'_*(\bar{x})}{2\mathbf{s}_*(\bar{x}) \cdot \mathbf{p}_*(\bar{x})}.$$

Then, noting Eq. (35), if $X_* = a$ we have

$$\frac{Q_0^\pm(X_* + \eta)}{Q_0^\pm(X_{**})} = \left(\frac{\mu_\lambda^\pm(X_{**})}{\mu_\lambda^\pm(X_* + \eta)}\right)^{1/4} \exp\left(\int_{X_* + \eta}^{X_{**}} I(\bar{x}) d\bar{x}\right) \sim \text{ord}\left(\frac{1}{\eta^{1/4}}\right). \tag{55}$$

The final observation arises from using a few previous results in combination. Firstly, we have that μ_λ^\pm is bounded away from zero by Proposition 5 and we recall that μ_λ^\pm is an eigenvalue of \mathbf{B}_λ , given by Eq. (44). Then Proposition 8, which also applies when $X_* = b$, gives the final result:

$$\frac{Q_0^\pm(X_* - \eta)}{Q_0^\pm(X_{**})} = \left(\frac{\mu_\lambda^\pm(X_{**})}{\mu_\lambda^\pm(X_* - \eta)}\right)^{1/4} \exp\left(-\int_{X_{**}}^{X_* - \eta} I(\bar{x}) d\bar{x}\right) \sim \text{ord}\left(\frac{1}{\eta^{1/4}}\right). \tag{56}$$

To match Dirichlet boundary conditions at $x = X_*$ we have, at the point $x = X_* + \sigma_{X_*}\eta$, that (using the arbitrary constants S_0^\pm and C_0^\pm) double angle formulae can be used to rewrite the trigonometric contribution to \mathbf{w}_\pm within the expression of Eq. (36) in the form

$$\begin{aligned} \widehat{S}_0^\pm \sin\left(\frac{1}{\varepsilon} \int_{X_*}^{x=X_* + \eta} \sqrt{\mu_\lambda^\pm(\bar{x})} d\bar{x}\right) &= \text{ord}\left(\frac{\eta}{\varepsilon}\right) = \text{ord}(\eta), & X_* = a \\ \widehat{S}_0^\pm \sin\left(\frac{1}{\varepsilon} \int_{x=X_* - \eta}^{X_*} \sqrt{\mu_\lambda^\pm(\bar{x})} d\bar{x}\right) &= \text{ord}\left(\frac{\eta}{\varepsilon}\right) = \text{ord}(\eta), & X_* = b \end{aligned} \tag{57}$$

as $\eta \rightarrow 0^+$, noting as above that μ_λ^\pm is bounded away from zero, and where \widehat{S}_0^\pm is a real constant. In particular, the analogous cosine contribution is set to zero by the imposition of the Dirichlet condition at $x = X_*$ and $\widehat{S}_0^\pm \neq 0$ to avoid the trivial solution. Eqs. (55), (56), and (57) then give

$$\mathbf{w}_\pm(X_* + \sigma_{X_*}\eta) = \text{ord}(\eta^{3/4}).$$

□

An immediate corollary of Proposition 9 is that if $a = 0$ or $b = 1$ (but not both), then we need to apply both a homogeneous Dirichlet condition to maintain boundedness, as above, and homogeneous Neumann conditions to satisfy the zero flux boundary conditions at the edge of the domain. Only the trivial solution is then possible, so we have that $a = 0$ and $b = 1$ are excluded from this class of solutions.

We further note that dealing with the case $X_* = b$ in addition to $X_* = a$ adds to the detail of the calculations required to deduce the above results, though not the concepts. One could alternatively deduce the result for $X_* = b$ with the approach to the singular point from below, from the result with $X_* = a$ with the approach to the singular point from above, as follows. In particular, with

$$x \rightarrow 1 - x, \quad \mathbf{J}(x) \rightarrow \mathbf{J}(1 - x), \quad \mathbf{D}(x) \rightarrow \mathbf{D}(1 - x),$$

and noting that $\mathbf{M}(x)$ and $\mathbf{N}(x)$ remain smooth and bounded under this mapping, a singularity approached from below at $X_* = b$ will be mapped to a singularity approached from above at $X_* = 1 - b$, but the scale of the singularity will be invariant. The latter will have \mathbf{w}_\pm scale with $\eta^{1/4}$, where $x = 1 - b + \eta$, and hence the singularity approached from below at $X_* = b$ of the original problem will also scale with $\eta^{1/4}$. Thus, one may alternatively only track the calculations for $X_* = a$ above and then infer the result for $X_* = b$ using this reasoning.

In addition, the following Proposition also demonstrates that if these conditions hold for real $\lambda_* > 0$, then they hold for all non-negative $\lambda < \lambda_*$.

Proposition 10. *Assume the homogeneous stability constraints of Eq. (23) are given. Then, if $\lambda_* > 0$ is permissible for $x \in (a, b)$, all $\lambda \in [0, \lambda_*]$ are permissible for $x \in (a, b)$.*

Proof. Recall that $\mathbf{B}_\lambda = \mathbf{D}^{-1}(\mathbf{J} - \lambda\mathbf{I})$ and hence

$$\text{tr}(\mathbf{B}_\lambda) = \text{tr}(\mathbf{D}^{-1}\mathbf{J}) - \lambda\text{tr}(\mathbf{D}^{-1}), \quad \det(\mathbf{B}_\lambda) = \det(\mathbf{D}^{-1})(\lambda^2 - \lambda(\text{tr}\mathbf{J}) + \det(\mathbf{J})).$$

Thus, for $\lambda_* > 0$ permissible with $\lambda_* > \lambda \geq 0$ we have

$$\text{tr}(\mathbf{B}_\lambda) = \text{tr}(\mathbf{B}_{\lambda_*}) + (\lambda_* - \lambda)\text{tr}(\mathbf{D}^{-1}) > \text{tr}(\mathbf{B}_{\lambda_*}) > 0,$$

noting λ_* is permissible and so $\text{tr}(\mathbf{B}_{\lambda_*}) > 0$ and $\text{tr}(\mathbf{D}^{-1}) > 0$ by positive definiteness of \mathbf{D} . Hence the first condition of Eq. (42) is satisfied for \mathbf{B}_λ .

We also need to ensure the second condition of Eq. (42) to demonstrate permissibility by Proposition 5. Hence we define

$$P(\lambda) := \text{tr}(\mathbf{B}_\lambda)^2 - 4\det(\mathbf{B}_\lambda) = \zeta_2\lambda^2 + \zeta_1\lambda + \zeta_0,$$

where

$$\zeta_2 = (\text{tr}(\mathbf{D}^{-1}))^2 - 4\det(\mathbf{D}^{-1}), \quad \zeta_1 = 4\det(\mathbf{D}^{-1})\text{tr}(\mathbf{J}) - 2\text{tr}(\mathbf{D}^{-1}\mathbf{J})\text{tr}(\mathbf{D}^{-1}),$$

$$\text{and } \zeta_0 = (\text{tr}(\mathbf{D}^{-1}\mathbf{J}))^2 - 4\det(\mathbf{D}^{-1}\mathbf{J}).$$

With η_1, η_2 the eigenvalues of \mathbf{D}^{-1} , which are real and positive by positive definiteness of \mathbf{D} , but conceivably repeated, note that

$$\zeta_2 = (\eta_1 - \eta_2)^2 \geq 0.$$

Furthermore, let

$$\lambda_1 = \frac{\operatorname{tr}(\mathbf{D}^{-1}\mathbf{J})}{\operatorname{tr}(\mathbf{D}^{-1})},$$

so that $\operatorname{tr}(\mathbf{B}_{\lambda_1}) = 0$. Thus $\lambda_2 \geq \lambda_1$ implies $\operatorname{tr}(\mathbf{B}_{\lambda_2}) \leq 0$, which in turn implies that λ_2 is not permissible by Proposition 5. Hence λ_* permissible gives $\lambda_* < \lambda_1$. Also, as $\lambda_* > 0$, we then have $\lambda_*^2 < \lambda_1^2$ and hence

$$\begin{aligned} P(\lambda_*) &= P(\lambda_1) + (\operatorname{tr}(\mathbf{D}^{-1}\lambda_* - \operatorname{tr}(\mathbf{D}^{-1}\mathbf{J}))^2 + 4\det(\mathbf{D}^{-1})(\lambda_1^2 - \lambda_*^2) \\ &\quad - 4\det(\mathbf{D}^{-1})\operatorname{tr}(\mathbf{J})(\lambda_1 - \lambda_*) > P(\lambda_1), \end{aligned}$$

using the homogeneous conditions of Eq. (23) and the positive definiteness of \mathbf{D} . Thus, if $\zeta_2 > 0$, then λ_* is on the decreasing branch of the quadratic $P(\lambda)$, as is any smaller value of λ since $P(\xi) \rightarrow \infty$ as $\xi \rightarrow -\infty$. Alternatively, if $\zeta_2 = 0$, we have the degenerate linear case for $P(\lambda)$ with a negative gradient. Either way, for $0 \leq \lambda < \lambda_*$ we have

$$P(\lambda) > P(\lambda_*) \geq 0$$

and the second condition Eq. (42) is satisfied for \mathbf{B}_λ and we have permissibility by Proposition 5. \square

4.3. Localized WKB solutions. We restrict ourselves to non-negative growth rates, λ , so that $\Re(\lambda) > 0$, while recalling that λ does not vary across the domain and must be such that μ_λ^\pm satisfies the constraint (39) and thus be permissible. Hence, by Proposition 3 we further have that λ is real. Given the equivalent conditions of permissibility of Eq. (42) from Proposition 5, Proposition 9 shows the behavior of the WKB leading order solutions near singular points, while Proposition 6 shows how to locate singular points for a given non-negative permissible growth rate, λ , from \mathbf{D} and \mathbf{J} . These propositions, and thus the form of the resulting solutions, require that

$$[\operatorname{tr}(\mathbf{B}_\lambda)]^2 - 4\det(\mathbf{B}_\lambda) \tag{58}$$

only has simple zeros, if any.

In general we have considered open intervals $(a, b) \subseteq (0, 1)$ where WKB leading order solutions for such λ exist, though in general the set on which they exist can be a union of such domains, and all of the above propositions apply. Thus we use the definition:

Definition 4.3. For $\lambda > 0$ we define \mathcal{T}_λ to be the closure of the maximal open set where λ is permissible.

In particular, \mathcal{T}_λ need not be simply connected. At its edges we also have either homogeneous Neumann conditions from the boundary conditions at $x \in \{0, 1\}$ or homogeneous Dirichlet conditions from Proposition 9 for internal edges, assuming these correspond to simple zeros of Eq. (58), noting a bounded non-trivial WKB leading order solution of the form of Eq. (36) is required for the solution to represent an unstable mode. Note that no singularities emerge from the denominator $[\mu_\lambda^\pm]^{1/4}$, as discussed at the start of Section 4.2. In addition, a final wave selection condition, such as Eq. (39), must be imposed across one of the intervals constituting \mathcal{T}_λ to ensure the homogeneous edge conditions at the edges of this interval can be

satisfied (for a suitable choice of sufficiently small ε and thus the diffusion scale). The WKB solution on all other intervals constituting \mathcal{T}_λ can then be set to the trivial zero solution. In addition, outside \mathcal{T}_λ , the lack of permissibility for λ entails non-trivial WKB leading order solutions cannot satisfy the waveform selection constraints required to fulfil the homogeneous conditions at the edges, \mathcal{T}_λ , leaving only the trivial WKB solution for the leading order solution in the complement of \mathcal{T}_λ .

Strictly, such solutions are only outer solutions and an inner solution would be required to generate a smooth leading order composite solution. However, the outer solutions are sufficient for our purposes.

Our results thus far, for the simple case that \mathcal{T}_λ is simply connected, may be represented by the following theorem for instability, directly analogous to that of [17], but now applicable to the more general cross-diffusion systems of Eq. (4)-(6), linearizing to Eq. (13).

Theorem 4.4 (λ -Dependent Heterogeneous Case). *Let $\Re(\lambda) > 0$, $0 < \varepsilon \ll 1$, and assume that*

$$[\text{tr}(\mathbf{B}_\lambda(x))]^2 - 4 \det(\mathbf{B}_\lambda(x))$$

has no more than two simple zeros for $x \in [0, 1]$, and is positive between these two zeros. We assume stability to perturbations in the absence of diffusion, i.e.,

$$\text{tr}(\mathbf{J}(x)) < 0, \det(\mathbf{J}(x)) > 0, \text{ for all } x \in [0, 1], \tag{59}$$

is given. Then there exists non-homogeneous, non-trivial, bounded perturbations \mathbf{w} satisfying Eq. (13) to leading order in ε , which grow as $e^{\lambda t}$ in the interval $x \in (a(\lambda), b(\lambda))$ if

$$\text{tr}(\mathbf{B}_\lambda(x)) > 0, [\text{tr}(\mathbf{B}_\lambda(x))]^2 - 4 \det(\mathbf{B}_\lambda(x)) > 0, \text{ for all } x \in (a(\lambda), b(\lambda)), \tag{60}$$

and ε satisfies the wave-selection constraint

$$\left(n^\pm + \frac{K}{2}\right) \pi \varepsilon = \int_{a(\lambda)}^{b(\lambda)} \sqrt{\mu_\lambda^\pm(\bar{x})} d\bar{x} \tag{61}$$

for any natural number $n^\pm > 0$, such that

$$a(\lambda) = \max(0, \min(\{x : [\text{tr}(\mathbf{B}_\lambda(x))]^2 - 4 \det(\mathbf{B}_\lambda(x)) = 0\})),$$

$$b(\lambda) = \min(1, \max(\{x : [\text{tr}(\mathbf{B}_\lambda(x))]^2 - 4 \det(\mathbf{B}_\lambda(x)) = 0\})),$$

and $K = 0$ if either $a(\lambda) = 0$ and $b(\lambda) = 1$, or if $0 < a(\lambda) < b(\lambda) < 1$; otherwise $K = 1$.

Proof. We have $\mathcal{T}_\lambda = (a(\lambda), b(\lambda))$. Also μ_λ^\pm is real and permissible on \mathcal{T}_λ by Propositions 2 and 5, while Eq. (44) and conditions (60) imply that μ_λ^\pm is positive on \mathcal{T}_λ . Further, by Proposition 3, we have no loss of generality in specializing to strictly real λ . Finally, by Proposition 9, we have that the WKB solutions can be bounded at any interior edges of \mathcal{T}_λ by homogeneous Dirichlet conditions at the interior edges of \mathcal{T}_λ , and the boundary conditions require homogeneous Neumann conditions.

The permissibility of μ_λ^\pm on \mathcal{T}_λ allows non-trivial leading-order WKB solutions on \mathcal{T}_λ . Conversely, noting the definition of permissibility, its absence on the complement of \mathcal{T}_λ implies that the wave selection constraint cannot be satisfied and thus there is only the trivial WKB solution on the complement of \mathcal{T}_λ . Thus we have the following solutions, classified by the possible forms of \mathcal{T}_λ , given

$$[\text{tr}(\mathbf{B}_\lambda(x))]^2 - 4 \det(\mathbf{B}_\lambda(x))$$

has no more than two simple zeros for $x \in [0, 1]$:

- no singular points, so $\mathcal{T}_\lambda = [0, 1]$ and the solution is

$$\begin{aligned} \mathbf{w}^\pm(x, t) &= e^{\lambda t} \exp\left(-\int_0^x \frac{\mathbf{s}_*^\pm(\bar{x})^T \mathbf{D}^{-1}(\bar{x}) \mathbf{M}(\bar{x}) \mathbf{p}_*^\pm(\bar{x}) + 2\mathbf{s}_*^\pm(\bar{x})^T (\mathbf{p}_*^\pm)'(\bar{x})}{2\mathbf{s}_*^\pm(\bar{x})^T \mathbf{p}_*^\pm(\bar{x})} d\bar{x}\right) \\ &\quad \times \frac{C_0^\pm}{[\mu_\lambda^\pm(x)]^{1/4}} \cos\left(\frac{1}{\varepsilon} \int_0^x \sqrt{\mu_\lambda^\pm(\bar{x})} d\bar{x}\right) \mathbf{p}_*(x), \end{aligned}$$

with

$$\int_0^1 \sqrt{\mu_\lambda^\pm(\bar{x})} d\bar{x} = n^\pm \pi \varepsilon; \quad (62a)$$

- one singular point $x_*(\lambda) > 0$, so without loss of generality, $(x_*, 1) = \mathcal{T}_\lambda$, with solution

$$\begin{aligned} \mathbf{w}^\pm(x, t) &= e^{\lambda t} \exp\left(\int_x^1 \frac{\mathbf{s}_*^\pm(\bar{x})^T \mathbf{D}^{-1}(\bar{x}) \mathbf{M}(\bar{x}) \mathbf{p}_*^\pm(\bar{x}) + 2\mathbf{s}_*^\pm(\bar{x})^T (\mathbf{p}_*^\pm)'(\bar{x})}{2\mathbf{s}_*^\pm(\bar{x})^T \mathbf{p}_*^\pm(\bar{x})} d\bar{x}\right) \\ &\quad \times \frac{S_0^\pm}{[\mu_\lambda^\pm(x)]^{1/4}} \sin\left(\frac{1}{\varepsilon} \int_{x_*}^x \sqrt{\mu_\lambda^\pm(\bar{x})} d\bar{x}\right) \mathbf{p}_{*\pm}(x), \end{aligned}$$

with

$$\int_{x_*}^1 \sqrt{\mu_\lambda^\pm(\bar{x})} d\bar{x} = \left(n^\pm + \frac{1}{2}\right) \pi \varepsilon, \quad (62b)$$

for $x \in \mathcal{T}_\lambda$, and zero otherwise;

- two singular points $x_*(\lambda), x_{**}(\lambda) \in (0, 1)$ delimiting the \mathcal{T}_λ set, i.e. $\mathcal{T}_\lambda = (x_*, x_{**})$, with solution

$$\begin{aligned} \mathbf{w}^\pm(x, t) &= e^{\lambda t} \exp\left(\int_{x_*(\lambda)}^{x_{**}(\lambda)} \frac{\mathbf{s}_*^\pm(\bar{x})^T \mathbf{D}^{-1}(\bar{x}) \mathbf{M}(\bar{x}) \mathbf{p}_*^\pm(\bar{x}) + 2\mathbf{s}_*^\pm(\bar{x})^T (\mathbf{p}_*^\pm)'(\bar{x})}{2\mathbf{s}_*^\pm(\bar{x})^T \mathbf{p}_*^\pm(\bar{x})} d\bar{x}\right) \\ &\quad \times \frac{S_0^\pm}{[\mu_\lambda^\pm(x)]^{1/4}} \sin\left(\frac{1}{\varepsilon} \int_x^{x_{**}} \sqrt{\mu_\lambda^\pm(\bar{x})} d\bar{x}\right) \mathbf{p}_{*\pm}, \end{aligned}$$

with

$$\int_{x_*(\lambda)}^{x_{**}(\lambda)} \sqrt{\mu_\lambda^\pm(\bar{x})} d\bar{x} = n^\pm \pi \varepsilon, \quad (62c)$$

for $x \in \mathcal{T}_\lambda$, and zero otherwise.

We note that requiring ε to satisfy the wave selection constraint ensures that the boundary conditions are satisfied, and hence the above expressions constructively give the non-trivial and bounded solutions required for the proof. \square

The generalization of Theorem 4.4 to more than two singular points and non-simply connected \mathcal{T}_λ is directly analogous, except for the wave selection criteria. One has two degrees of freedom, λ and ε , so it should be feasible to simultaneously satisfy two wave selection constraints from distinct simply connected intervals \mathcal{T}_λ . However, the ability to satisfy higher numbers of constraints simultaneously is unclear, potentially limiting the number of distinct simply connected regions where a single WKB solution has support (though of course the full solution to Eq. (13) will involve a superposition of different modes on different regions \mathcal{T}_λ). One final important result is the monotonicity of \mathcal{T}_λ with respect to λ , which follows in exactly the same way as presented in [17], which we repeat here for completeness:

Proposition 11. *If $\mathcal{T}_{\lambda_2} \neq \emptyset$ and $0 \leq \lambda_1 \leq \lambda_2$, then $\mathcal{T}_{\lambda_2} \subseteq \mathcal{T}_{\lambda_1}$. If $\mathcal{T}_{\lambda_1} \neq [0, 1]$, and $0 \leq \lambda_1 < \lambda_2$, then we have the stricter inclusion $\mathcal{T}_{\lambda_2} \subset \mathcal{T}_{\lambda_1}$.*

Proof. The first part of this result, for $0 \leq \lambda_1 \leq \lambda_2$, follows from Proposition 10. Hence we need to show that if $\lambda_1 < \lambda_2$, then \mathcal{T}_{λ_2} is a strict subset of \mathcal{T}_{λ_1} if $\mathcal{T}_{\lambda_1} \neq [0, 1]$. We note that the internal edges of \mathcal{T}_λ are zeros with respect to x of

$$(\text{tr}\mathbf{B}_\lambda(x))^2 - 4 \det(\mathbf{B}_\lambda(x)).$$

Also, differentiating with respect to λ for $\lambda \geq 0$ gives

$$\frac{\partial}{\partial \lambda} [(\text{tr}\mathbf{B}_\lambda(x))^2 - 4 \det(\mathbf{B}_\lambda(x))] = -2\text{tr}(\mathbf{B}_\lambda)\text{tr}(\mathbf{D}^{-1}) + 4\text{tr}(\mathbf{J}_\lambda) \det(\mathbf{D}^{-1}) < 0, \tag{63}$$

which follows by determining the sign of each term (all traces and determinants are positive except for $\text{tr}(\mathbf{J}_\lambda) < \text{tr}(\mathbf{J}) < 0$). As $(\text{tr}\mathbf{B}_\lambda(x))^2 - 4 \det(\mathbf{B}_\lambda(x)) > 0$ for x in the interior of \mathcal{T}_λ , reducing λ_2 increases the value of

$$\text{tr}(\mathbf{B}_{\lambda_2}(x))^2 - 4 \det(\mathbf{B}_{\lambda_2}(x)) \tag{64}$$

at any given point x . Hence if an open simply connected region within \mathcal{T}_{λ_2} is given by $a(\lambda_2) < x < b(\lambda_2)$, we have that if $0 \leq \lambda_1 < \lambda_2$ and $a(\lambda_2) > 0$, so that the edge point is in the interior of the domain and thus a zero of Eq. (64), then $a(\lambda_1) < a(\lambda_2)$. Similarly, given the above ordering of λ_1 and λ_2 , if $b(\lambda_2) < 1$ then $b(\lambda_1) > b(\lambda_2)$, so the strict inclusion $\mathcal{T}_{\lambda_2} \subset \mathcal{T}_{\lambda_1}$ for $\mathcal{T}_{\lambda_1} \neq [0, 1]$ follows. \square

4.4. **Theorem 2.1:** We are now in a position to prove Theorem 2.1:

Proof. By Proposition 3, we can specialize to non-negative growth rates, λ , that are real. We consider \mathcal{T}_0 , which by the conditions, Eqs. (23) and (24), given in the theorem is non-empty, and by the inclusion result, Proposition 11, contains \mathcal{T}_λ for any non-negative λ . Continuity ensures that there exists sufficiently small $\lambda > 0$ such that \mathcal{T}_λ is non-empty and the simple zeros of \mathcal{T}_0 continuously map to simple zeros of \mathcal{T}_λ as λ is continuously shifted away from zero.

If we further have the limitation that

$$[\text{tr}(\mathbf{B}_\lambda(x))]^2 - 4 \det(\mathbf{B}_\lambda(x))$$

has no more than two simple zeros for $x \in [0, 1]$ with \mathcal{T}_λ simply connected for any such λ , then Theorem 4.4 gives leading order (in ε) WKB solutions, \mathbf{w}_\pm , of Eq. (62), that satisfy the requirements of Theorem 2.1. In particular, they are non-trivial, inhomogeneous, bounded and will drive an instability on $\mathcal{T}_\lambda \subseteq \mathcal{T}_0$ providing the wave selection criterion, as given by Eq. (61), can be satisfied. In particular, noting Eq. (3) and Eq. (61), continuously reducing the diffusion scale D to be sufficiently small and thus continuously reducing ε , will locate a value of D for which the wave selection criterion can be satisfied.

For the more general case where

$$[\text{tr}(\mathbf{B}_\lambda(x))]^2 - 4 \det(\mathbf{B}_\lambda(x))$$

can have more than two simple zeros for $x \in [0, 1]$ and/or \mathcal{T}_λ is not necessarily simply connected, we can similarly construct leading order WKB solutions of the form of \mathbf{w}_\pm in Eq. (62), with a wave selection constraint of the form of Eq. (61) for each simply connected region making up \mathcal{T}_λ . One, of many possible, wave selection criteria for this solution then is the constraint of satisfying the wave selection criterion on one, and only one, of the simply connected regions making up \mathcal{T}_λ . As this is, once more, a single simply connected region it can be achieved by continuously reducing the diffusion scale ε to be sufficiently small, as above. An associated leading order WKB solution can be constructed by taking it to be trivial on the other simply

connected regions constituting \mathcal{T}_λ and of the form of \mathbf{w}_\pm in Eq. (62) for the simply connected region where the wave selection criterion is satisfied. This provides leading order WKB solutions with the appropriate properties of being non-trivial, inhomogeneous and bounded, as required to demonstrate the theorem. \square

Note that the conditions of Theorem 2.1, with the homogeneous stability condition of Eq. (23) for $x \in [0, 1]$ and the inhomogeneous condition of Eq. (24) on at least a subset of $x \in [0, 1]$, directly generalize both the homogeneous conditions of Proposition 1 and the reaction-diffusion system without cross-diffusion studied in [17]. Thus Turing instability conditions generalize to inhomogeneous cross-diffusion systems, of which chemotaxis is a special case, with the very weak additional requirement that any zeros of $[\text{tr}(\mathbf{B}_0(x))]^2 - 4 \det(\mathbf{B}_0(x))$ are simple, noting zeros are excluded from the homogeneous case by Eq. (24).

Furthermore, by inspection of Eq. (61), there are countably infinite values of the diffusion scale, D , or equivalently ε , where the wave selection criterion is satisfied. One may also trivially note from the proof of Theorem 2.1 that when \mathcal{T}_0 is more complex, in particular not simply connected, there is a collection of WKB solutions of the form of Eq. (62) for each simply connected region constituting \mathcal{T}_λ and trivial elsewhere, generating multiple leading order WKB solutions. Once we have that regions given by the zeros of $[\text{tr}(\mathbf{B}_0(x))]^2 - 4 \det(\mathbf{B}_0(x))$ are not simply connected, delimiting when the wave selection criteria on more than one simply connected constituent of \mathcal{T}_λ can be *simultaneously* satisfied requires quantitative knowledge of the eigenvalues μ_λ^\pm , which we have not considered. However, we still anticipate being able to satisfy wave selection criteria on two simply connected constituents of \mathcal{T}_λ as there are two degrees of freedom, namely λ and, for example via changes in the diffusion scale, ε , that can be adjusted. More generally, this demonstrates the prospect of an even more extensive class of leading order WKB solutions, which have support on more than one simply connected domain and highlights rich possibilities of unstable leading order WKB solutions for more complex \mathcal{T}_λ . Such possibilities, as well as a more general study of these systems and the instability conditions, will be numerically explored in the following sections, where we explicitly demonstrate that heterogeneity can serve to localize patterns to regions predicted by the simple inequalities in Theorem 2.1.

5. Numerical results. We have built a general MATLAB code to solve (4) numerically, as well as to compute the boundaries of \mathcal{T}_0 where we expect to find deviations from our approximate steady state given by $\mathbf{f}(\mathbf{u}^*, x) = \mathbf{0}$. The code implements a method-of-lines discretization of the cross-diffusion terms given by

$$\frac{\partial}{\partial x} \left(D(u, v, x) \frac{\partial u}{\partial x} \right) \approx \frac{(u_{i+1} - u_i)(D_{i+1} + D_i) - (u_i - u_{i-1})(D_i + D_{i-1})}{2\delta x^2}, \quad (65)$$

where $D_i = D(u_i, v_i, x_i)$ with the subscript indicating evaluation at the i th grid point, and $\delta x = 1/(N - 1)$ with N denoting the number of grid points. The resulting system of ODEs is integrated using the MATLAB function `ode15s`, which implements a variable-step, variable-order solver [38]. Relative and absolute tolerances are taken to be 10^{-11} and a Jacobian sparsity pattern was used to speed up timestepping. Unless otherwise noted, $N = 10^4$ equispaced grid points are used. Convergence checks in the number of grid points and the maximum timestep were used for selected simulations to ensure soundness of the method. In all cases we used initial data of the form $u(0, x) = u^*(x)\xi_u(x)$, $v(0, x) = v^*(x)\xi_v(x)$, with ξ_u, ξ_v

being normal random variables with mean 1 and standard deviation 0.1 independently and identically at each spatial point. The code can be found at [18], and we encourage the interested reader to explore other systems and parameter regimes than those we report here.

To demonstrate the generality of our theory, we study three examples of cross-diffusion and its impact on pattern formation. Firstly we consider the Schnakenberg model [37, 29] with linear cross-diffusion terms [8],

$$\begin{aligned} \frac{\partial u}{\partial t} &= \varepsilon^2 \frac{\partial}{\partial x} \left(D_{11}(x) \frac{\partial u}{\partial x} + D_{12}(x) \frac{\partial v}{\partial x} \right) + a(x) - u + u^2 v, \\ \frac{\partial v}{\partial t} &= \varepsilon^2 \frac{\partial}{\partial x} \left(D_{21}(x) \frac{\partial u}{\partial x} + D_{22}(x) \frac{\partial v}{\partial x} \right) + b(x) - u^2 v, \end{aligned} \tag{66}$$

where we assume $a(x) > 0, b(x) > 0$ for all $x \in [0, 1]$. The approximate steady state is given by $u^*(x) = a(x) + b(x)$ and $v^*(x) = b(x)/(a(x) + b(x))^2$.

We also consider a version of the Keller-Segel model of chemotaxis [13, 11, 29, 10], noting that spatially heterogeneous variants have been studied in [47] and references therein. Accounting for logistic cell growth and linear chemoattractant dynamics, the model is given by

$$\begin{aligned} \frac{\partial u}{\partial t} &= \varepsilon^2 \frac{\partial}{\partial x} \left(D_{11}(x) \frac{\partial u}{\partial x} - \chi(x) u \frac{\partial v}{\partial x} \right) + u \left(1 - \frac{u}{K(x)} \right), \\ \frac{\partial v}{\partial t} &= \varepsilon^2 \frac{\partial}{\partial x} \left(D_{22}(x) \frac{\partial v}{\partial x} \right) + h(x) u - v, \end{aligned} \tag{67}$$

where we assume $K(x) > 0, h(x) > 0$ and $\chi(x) > 0$ for all $x \in [0, 1]$. The approximate steady state is given by $u^*(x) = K(x), v^*(x) = h(x)K(x)$.

Finally we explore the classical Shigesada-Kawasaki-Teramoto (SKT) model [39, 30, 25, 6, 35], with spatially heterogeneous variations studied in [23] and elsewhere. After a suitable rescaling, this model can be written² in a cross-diffusion form given by

$$\begin{aligned} \frac{\partial u}{\partial t} &= \varepsilon^2 \frac{\partial}{\partial x} \left((d_1(x) + d_{11}(x)u + d_{12}(x)v) \frac{\partial u}{\partial x} + d_{12}(x)u \frac{\partial v}{\partial x} \right) + r_1(x)u(1 - a_1(x)u - b_1(x)v), \\ \frac{\partial v}{\partial t} &= \varepsilon^2 \frac{\partial}{\partial x} \left(d_{21}(x)v \frac{\partial u}{\partial x} + (d_2(x) + d_{21}(x)u + d_{22}(x)v) \frac{\partial v}{\partial x} \right) + r_2(x)v(1 - b_2(x)u - a_2(x)v), \end{aligned} \tag{68}$$

where we assume that the kinetic functions $r_i(x) > 0, a_i(x) > 0$ and $b_i(x) > 0$ for all $x \in [0, 1]$. We will also assume that $a_1(x) > b_2(x)$, and $a_2(x) > b_1(x)$ to ensure the feasibility and stability (in the absence of transport) of an approximate coexistence equilibrium given by $u^*(x) = (a_2(x) - b_1(x))/(a_1(x)a_2(x) - b_1(x)b_2(x))$, $v^*(x) = (a_1(x) - b_2(x))/(a_1(x)a_2(x) - b_1(x)b_2(x))$.

In all cases we assume that the kinetic parameters are chosen so that our approximate heterogeneous steady states, \mathbf{u}^* , satisfy the boundary conditions (6). This is not strictly needed for the parameters r_i in the SKT model, as these do not enter into our approximate steady states. We do not make any explicit restrictions on the cross-diffusion parameters, except that \mathbf{D} must remain positive definite. We note, however, that the existence and regularity theory for these systems is much more intricate than for simpler reaction-diffusion models, with blow-up and singularities

²Starting from the original SKT model with a heterogeneous diffusion tensor, one may also obtain an ‘advection’ term involving first-order derivatives in u and v . For simplicity we will neglect these terms, as they do not arise in almost all other work on the SKT model when the diffusion tensor does not depend on x .

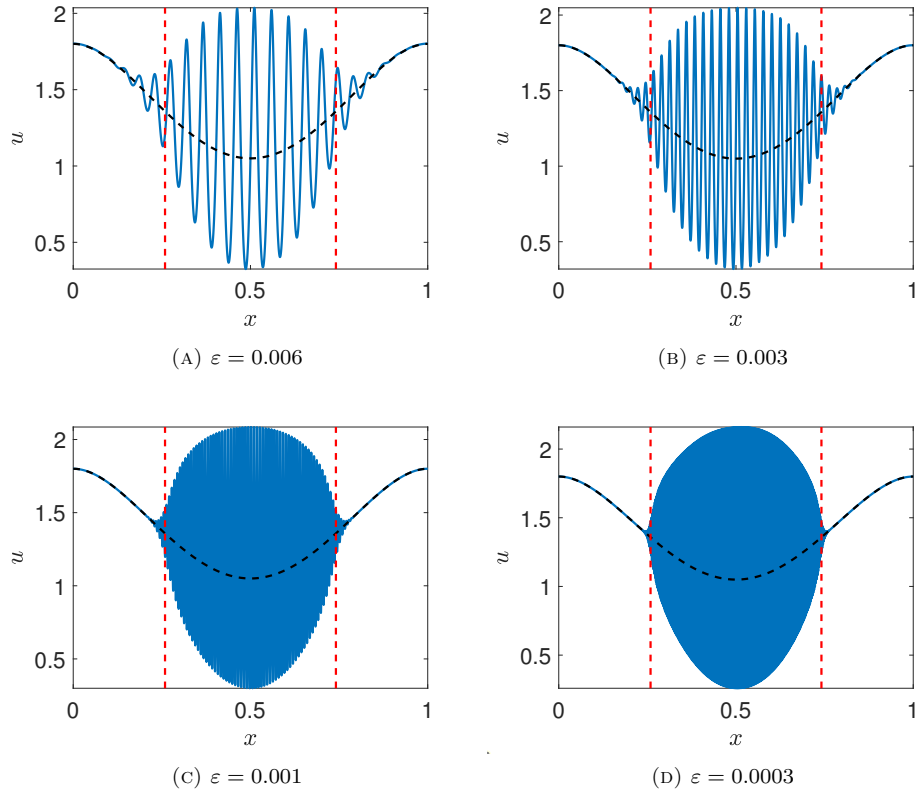


FIGURE 1. Plots of u in blue curves and u^* in dashed black curves from solutions of the Schnakenberg model, Eq. (66), for various values of ε at $t = 5,000$, which are essentially at steady state. The red vertical lines show the boundary of \mathcal{T}_0 computed from the conditions in Theorem 2.1. The parameters are taken as $a(x) = 0.8 - 12x^2(x-1)^2$, $b = 1$, $D_{11} = D_{22} = D_{12} = 1$, $D_{21} = 3((x-0.5)^2 - 1)$. Note that in panel (D), $N = 5 \times 10^4$ grid points were used to accurately represent the solution.

having a significant literature [6, 25, 23, 47]; see [24] for an introductory review to these complexities and their analysis.

We start by exploring the Schnakenberg model, Eq. (66), in a regime where the pure reaction-diffusion system would not pattern, namely when $D_{11} = D_{22} = 1$. We make $a(x)$ and $D_{21}(x)$ depend on space in such a way as to localize patterns to the interior of the domain, noting that $a(x)$ must satisfy the boundary conditions but $D_{21}(x)$ need not. We plot our numerical simulations in Fig. 1 for decreasing values of ε . The solution is shown at time $t = 5,000$, but in all cases is indistinguishable from the solution at $t = 200$, hence this appears to be an approximate (patterned) steady state. As anticipated by the theory, the location of the Turing regime \mathcal{T}_0 approximates where deviations from the heterogeneous steady state occur, and this approximation becomes better as ε decreases, with the number of

internal ‘spikes’ in the pattern increasing. This localization was shown for relatively simple heterogeneities in [17], and so we will now consider more elaborate examples.

The heterogeneities used in Fig. 1 were symmetric about the midpoint of the domain $x = 0.5$. We next consider an example with an asymmetric heterogeneity in $D_{12}(x)$, but otherwise use the same parameters. We show solutions for decreasing ε in Fig. 2, and now include kymographs (space-time plots) showing the evolution of u over time. Unlike the previous example, the solutions do not reach an apparent steady state but now move in the direction of increasing $D_{12}(x)$. The speed of these moving spikes is influenced by ε with extremely slow movement seen in panels (D) and especially (F). We expect that this movement is due to the kind of heterogeneity-induced spike oscillations reported in [32], which were later studied and explained in terms of spike generation and annihilation in [14, 21]. Despite the spatiotemporal nature of the solutions, the boundaries of \mathcal{T}_0 still give a good approximation for where the deviations from the steady state u^* occur.

Finally we consider a more intricate example with complex heterogeneities in both cross-diffusion parameters, $a(x)$ and $b(x)$ in Fig. 3. There are now four regions where Theorem 2.1 predicts pattern formation. However, for sufficiently large ε , wavemode selection prevents the rightmost of these regions from patterning in panels (A) and (B). As in Fig. 2, solutions within each region are spatiotemporally moving spikes, with speeds varying with ε but also with speed and direction dependent on the local heterogeneity. In particular, the local speed of a spike decreases with increasing x , and the direction of movement is always from lower values of u^* to higher values. We also observe an increase in the local frequency of oscillations with increasing x (see especially the leftmost and rightmost patterned regions in panels (C) and (E)).

We next consider simulations of the Keller-Segel chemotaxis system, Eq. (67). We show example steady state behaviors in Fig. 4 for heterogeneous $h(x)$, $K(x)$ and $\chi(x)$. While there is a size and wavelength modulation, and the patterned region is asymmetrically shaped, such solutions are steady in time. In contrast, if we let either $\chi(x) = 0$ or $h(x) = 0$, we observe the more complicated spatiotemporal behavior in Fig. 5 for sufficiently small ε . The direction of spike movement in either case is opposite, which helps explain why their combination leads to steady spikes in Fig. 4. Interestingly, while the spike movement decreases with decreasing ε , for $\varepsilon = 0.02$, no spike movement is observed in panels (A) and (B) of Fig. 5. This is consistent with observations of heterogeneous reaction-diffusion systems in [21], as such spike oscillations arise due to a global bifurcation structure involving spike creation and annihilation.

We now demonstrate localized pattern formation in the SKT model given by Eq. (68). We consider heterogeneous kinetic and diffusion parameters in Fig. 6, observing again that while localization occurs approximately within the bounds predicted by Theorem 2.1, there is spike movement for sufficiently small ε . We note that the spike speed decreases for decreasing values of ε , and spike wavelength, amplitude, and speed are spatially-dependent. We also observe in panel (B) that for sufficiently large ε , stationary patterns are observed in part of the domain, while spatiotemporal movement is still observed in another region. For $\varepsilon \geq 0.007$, there is no longer any spike movement and all of the solutions we found tended to stationary spatial profiles.

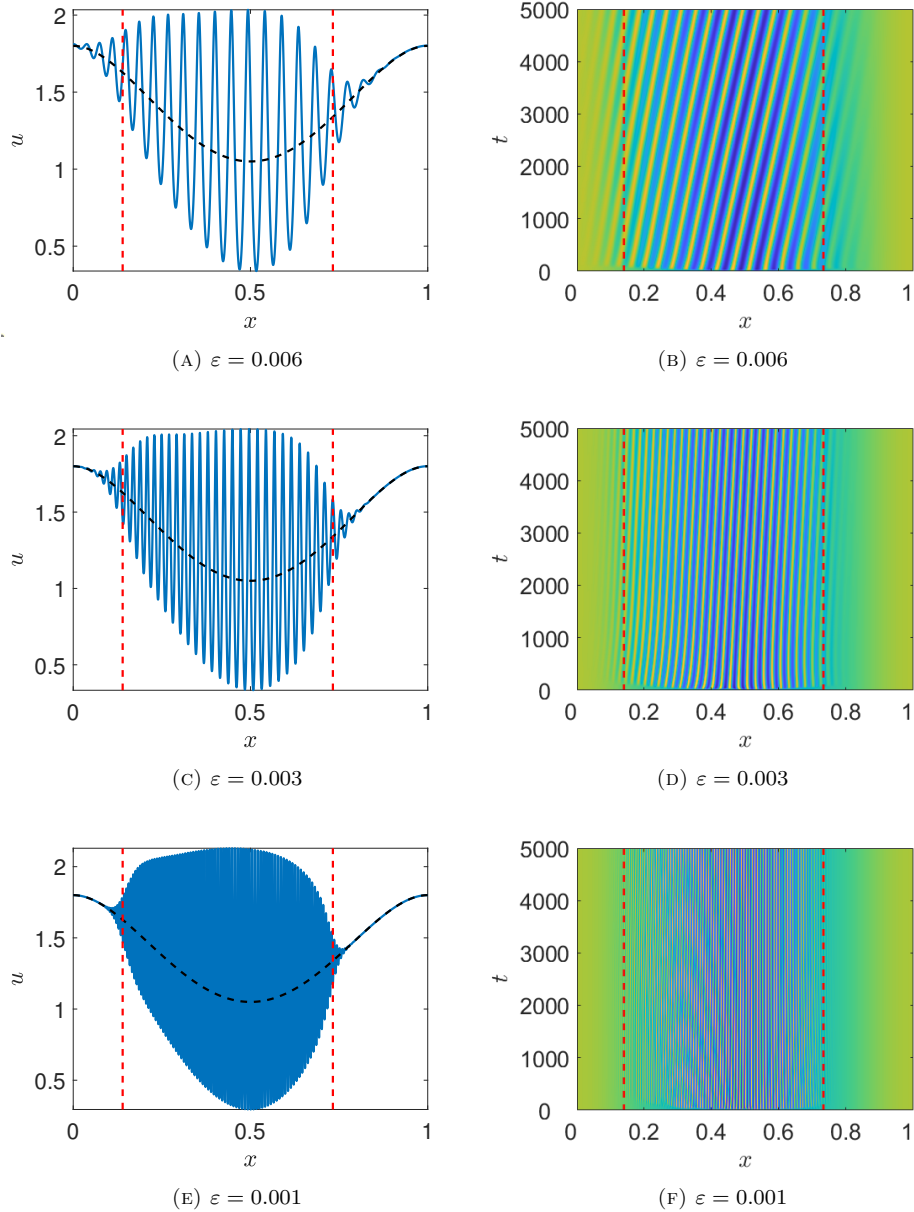


FIGURE 2. Plots of u in blue curves and u^* in dashed black curves from solutions of the Schnakenberg model, Eq. (66), for various values of ε at $t = 5,000$ in (A), (C), (E), and kymographs of u in (B), (D), (F). The red vertical lines show the boundary of \mathcal{T}_0 computed from the conditions in Theorem 2.1. The parameters are taken as $a(x) = 0.8 - 12x^2(x-1)^2$, $b = 1$, $D_{11} = D_{22} = 1$, $D_{12} = 0.5 + 0.8x$, $D_{21} = 3((x-0.5)^2 - 1)$.

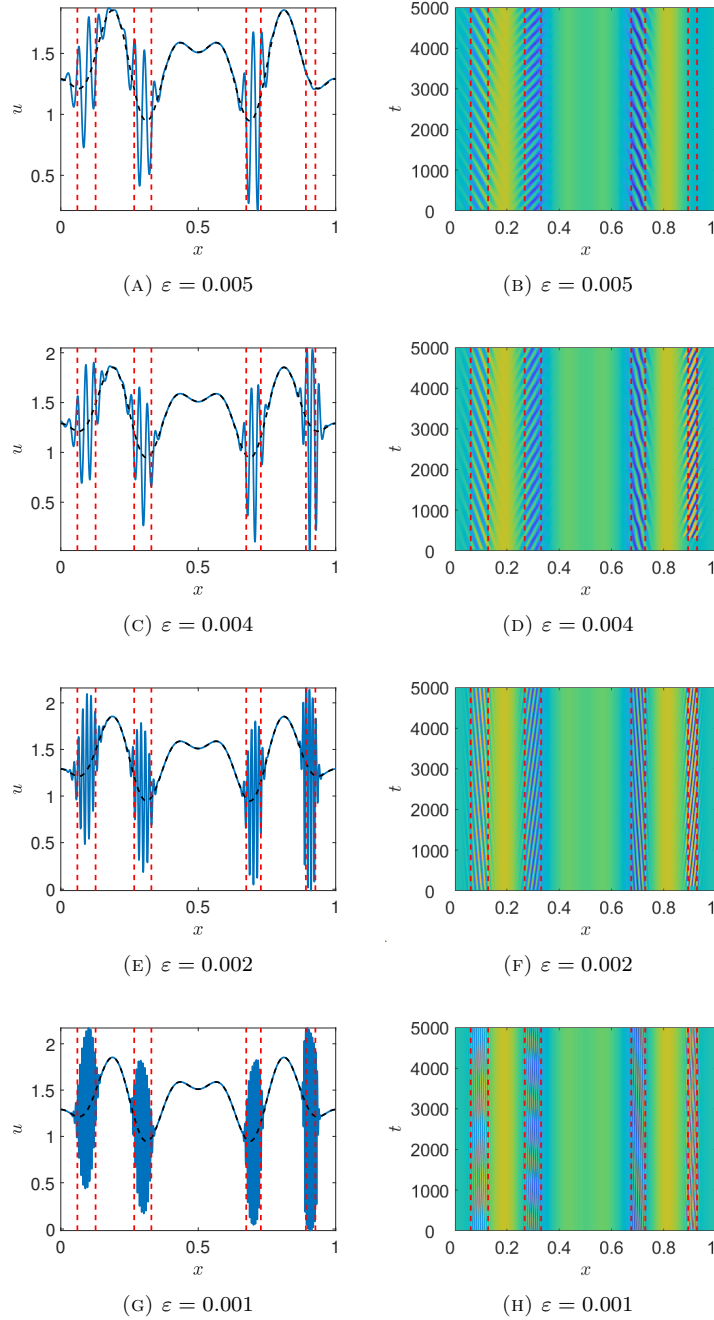


FIGURE 3. Plots of u in blue curves and u^* in dashed black curves from solutions of the Schnakenberg model, Eq. (66), for various values of ε at $t = 5000$ in (A), (C), (E), and kymographs of u in (B), (D), (F). The red vertical lines show the boundary of \mathcal{T}_0 computed from the conditions in Theorem 2.1. The parameters are taken as $a(x) = 0.01 + 0.19(1 + \cos(10x\pi))$, $b = 0.9 + 0.3(1 - \cos(6x\pi))$, $D_{11} = D_{22} = 1$, $D_{12} = 1 + \sin(3x\pi)$, $D_{21} = 2(x - 1)$.

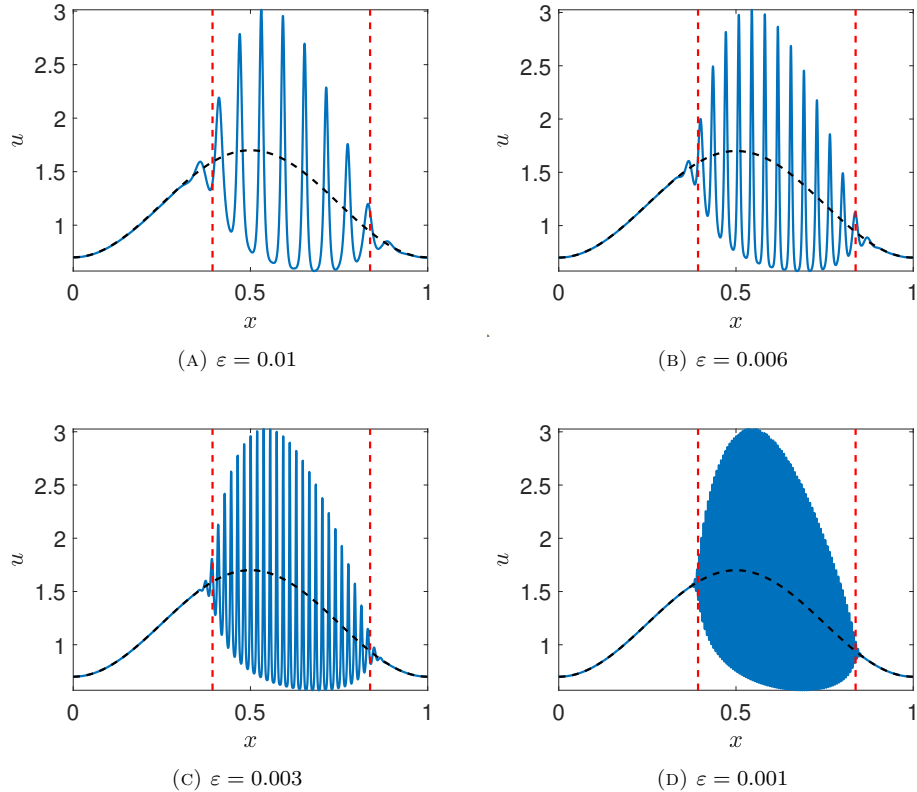


FIGURE 4. Plots of u in blue curves and u^* in dashed black curves from solutions of the Keller-Segel model, Eq. (67), for various values of ε at $t = 50,000$. The red vertical lines show the boundary of \mathcal{T}_0 computed from the conditions in Theorem 2.1. The parameters are taken as $K(x) = 1.2 - 0.5 \cos(2\pi x)$, $h(x) = (1 - 0.5 \cos(\pi x))$, $D_{11} = D_{22} = 1$, and $\chi(x) = 3.05 - 0.1x$.

6. Discussion. We have generalized the results found in [17] to nonlinear reaction-cross-diffusion systems. Our main result, presented in Theorem 2.1, can be interpreted as giving the locations where we expect pattern formation which is emergent from a Turing-type instability, as opposed to spatial structure arising from background heterogeneity itself. Such a distinction is a key result of our linear theory. We numerically validated this theory using a wide variety of cross-diffusion models, finding an excellent agreement with the analytical predictions for sufficiently small ε . We also showed that numerical instabilities arising from spike instabilities and creation will also remain within the spatial regions predicted by our instability analysis, though our theory cannot differentiate between steady state pattern formation and such spatiotemporal oscillations.

There are many avenues for future work, particularly where we think the main approach presented may be especially tractable. In principle our theory of pattern localization should extend to systems where all spatial derivatives of order n are scaled with ε^n , such as in fourth-order pattern forming models like Swift-Hohenberg

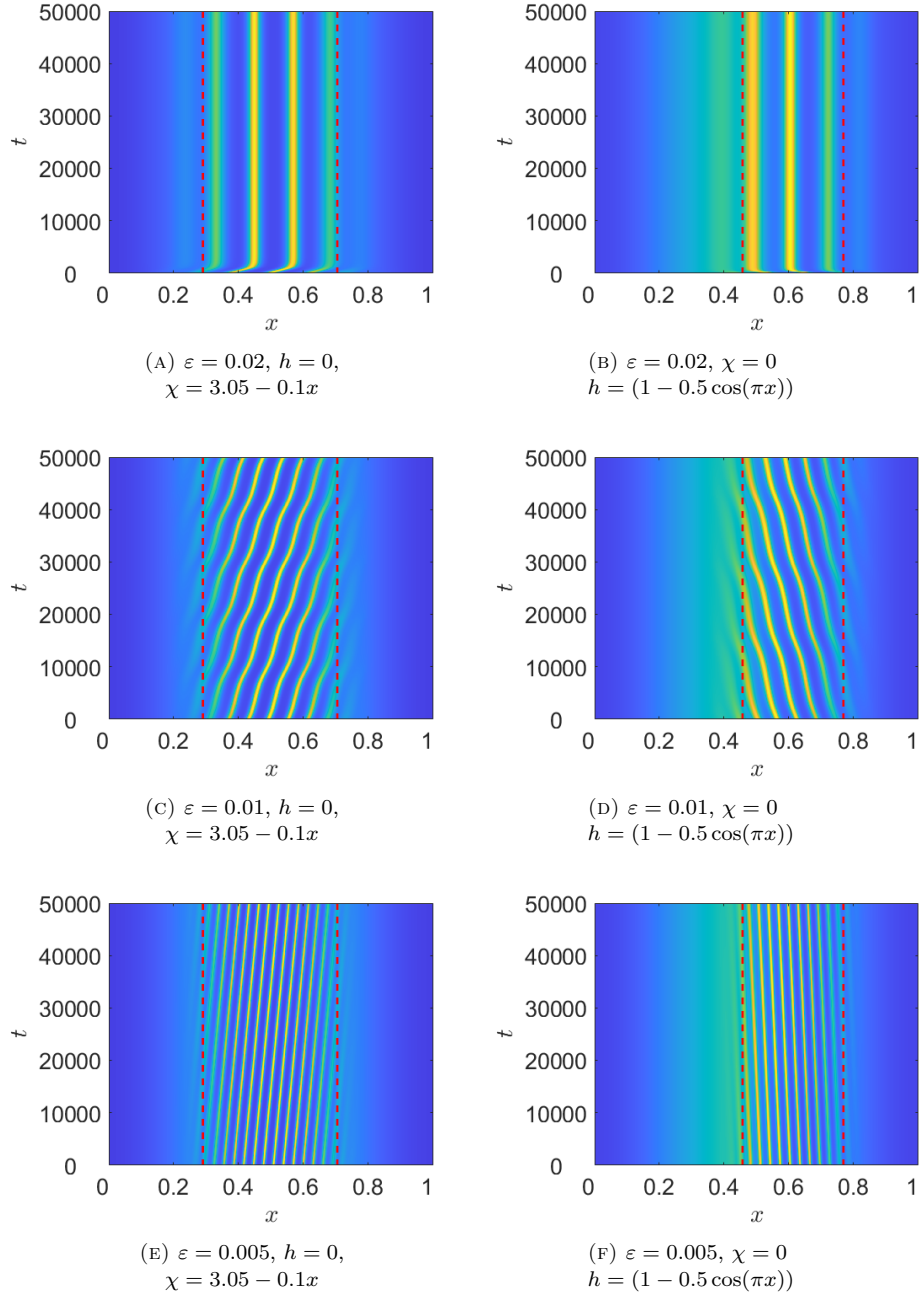


FIGURE 5. Plots of u from solutions of the Keller-Segel model, Eq. (67), for various values of ε at $t = 50,000$. The red vertical lines show the boundary of \mathcal{T}_0 computed from the conditions in Theorem 2.1. The parameters are taken as $K(x) = 1.2 - 0.5 \cos(2\pi x)$ and $D_{11} = D_{22} = 1$.

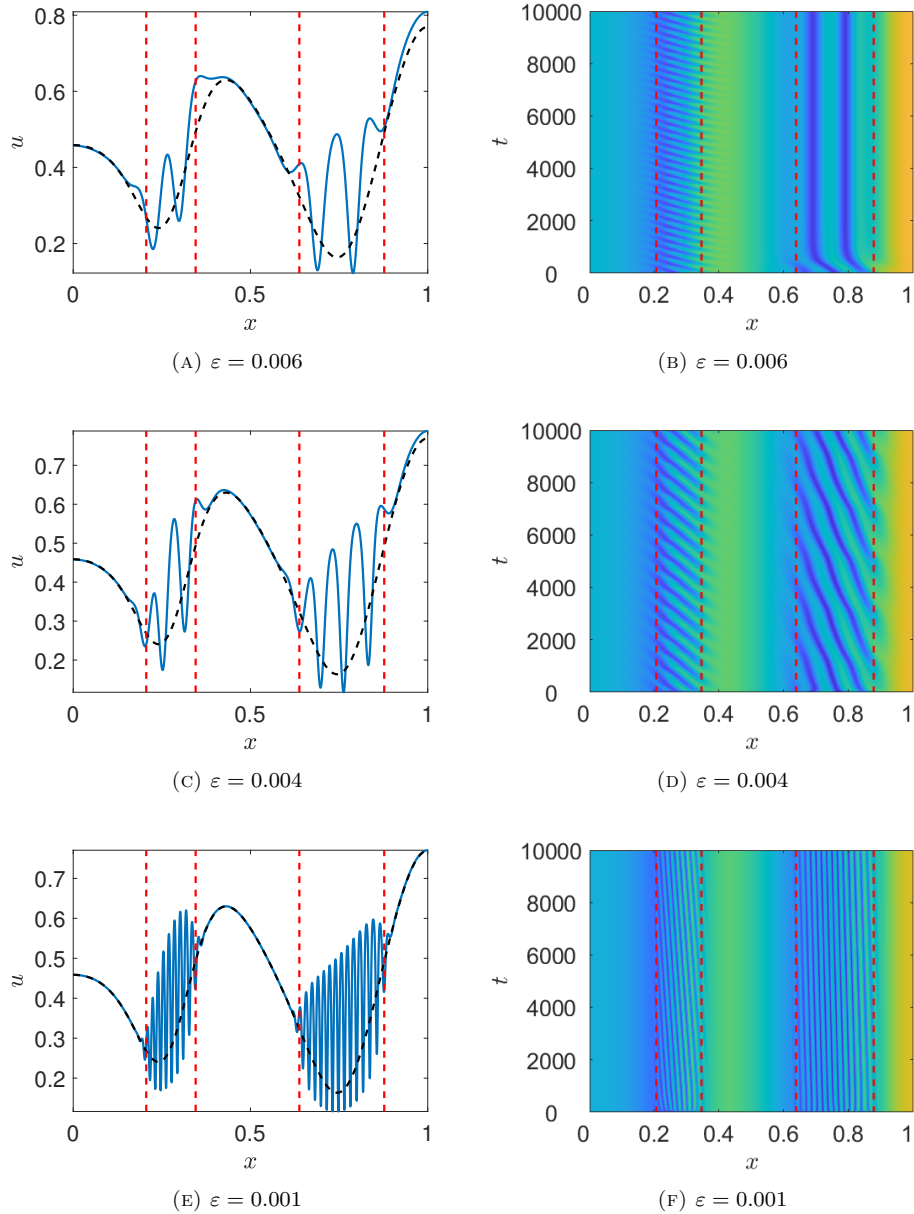


FIGURE 6. Plots of u in blue curves and u^* in dashed black curves from solutions of the SKT model, Eq. (68), for various values of ε at $t = 50,000$ in (A), (B), (E), and kymographs of u in (B), (D), (F). The red vertical lines show the boundary of \mathcal{T}_0 computed from the conditions in Theorem 2.1. The parameters are taken as $r_1(x) = 1$, $r_2(x) = 2$, $a_1(x) = 0.9 + 0.2 \cos(3\pi x)$, $a_2(x) = 0.9 + 0.2 \cos(4\pi x)$, $b_1(x) = 0.6$, $b_s(x) = 0.2$, $d_1(x) = d_2(x) = 1$, $d_{21}(x) = 200x$, $d_{11}(x) = d_{12}(x) = d_{22}(x) = 0$.

or Cahn-Hilliard systems. Such a setting may actually be an easier context in which to pursue weakly nonlinear analyses to study the saturation of pattern amplitude as a function of the growth rate λ , and potentially to explore questions of spatiotemporal oscillations. Numerical continuation could help connect the theory developed here to other kinds of localized patterns, such as localized patterns found via nonlinear mechanisms such as homoclinic snaking [41, 1]. An interesting question would be how these different kinds of localized structures interact.

Extending these results to more than two species, as has been well-studied in the spatially homogeneous setting [36], is in principle straightforward, though the calculations may become overly cumbersome. A more difficult challenge, and one for which we have no easy way to extend the theory, is to prove analogous results for higher spatial dimensions. Numerically, we have explored such extensions and found excellent agreement with the expected localization [46], but the WKB approach becomes substantially more technical to use in higher dimensions. We anticipate that there is an alternative way to prove something analogous to Theorem 2.1 which can be extended to higher dimensions. There are also aspects of our theory which deserve a more careful rigorous development, which others have begun [15].

While the details of our approach are somewhat technical, the overall results are intuitive, and in some sense can be viewed as justifying the ‘obvious’ localization one might anticipate in the regime of small ε . Nevertheless, our framework opens up a variety of ways of thinking of localization in pattern forming systems, which we think has ample use in developmental biological and ecological settings. The model Eq. (4) inherently contains two scale-separation assumptions. The explicit assumption in ε is that the diffusive scaling is smaller than that of the reaction (and that gradients in heterogeneous reactions are sufficiently slow). A second inherent assumption, however, is a timescale separation between the proposed pattern-forming model and whatever led to the pre-patterned state giving rise to the explicit spatial heterogeneities. Determining when these assumptions are valid, or how to conceptualize these systems when these assumptions are relaxed, is another key area of future work.

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