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Asymptotic Methods for Reaction-Diffusion Systems: Past and Present

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Abstract A brief historical survey of the development of asymptotic and analytical methodologies for the analysis of spatio-temporal patterns in reaction-diffusion (RD) and related systems is given. Although far from complete, the bibliography is hopefully representative of some of the advances in this area over the past 40 years. Within the scope of this survey, some of the key research contributions of Lee Segel are highlighted.

Keywords Multi-scale analysis · Amplitude equations · Singular perturbations · Interfacial patterns

A two-component RD system with general reaction kinetics f and g has the form

$$u_t = D_u \Delta u + f(u, v), \qquad v_t = D_v \Delta v + g(u, v). \tag{1}$$

On a bounded domain with no-flux boundary conditions, the pioneering study of Alan Turing (cf. Turing, 1952) showed that a spatially homogeneous steady-state solution of (1) that is stable in the absence of diffusion can be de-stabilized in the presence of unequal diffusivities in (1) when a control parameter in the kinetics is varied. The onset of such a Turing instability is characterized by the creation of a small-amplitude spatial pattern with a certain spatial wavelength. Away from the conditions for the onset of a Turing instability, (1) can support finite-amplitude spatio-temporal patterns of remarkable diversity and complexity. Detailed studies of pattern formation for (1) have been made for many specific forms of the kinetics f and g, including the classical Gierer–Meinhardt (GM) model $f = -u + u^2/v$, $g = -v + u^2$ (cf. Gierer and Meinhardt, 1972), the Gray–Scott

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(GS) model $f = -u + avu^2$, $g = (1 - v) - vu^2$ (cf. Pearson, 1993), the Brusselator model $f = a - (b + 1)u + u^2 v$, $g = bu - u^2 v$ (cf. Nicolis and Prigogine, 1977); and the Fitzhugh–Nagumo model $f = u(u - a)(1 - u) - v$, $g = u - cv$, where $0 < a < 1$. A survey of mathematical modeling of biological and chemical phenomena using RD systems is given in Maini et al. (1997). Mathematical modeling of patterns in biological morphogenesis using extensions of the GM model are discussed at length in Koch and Meinhardt (1994), Meinhardt (1982), and Meinhardt (1995). The possibility of a Turing instability for a diffusive ecological-interaction model with certain predatory-prey kinetics was studied by Lee Segel in Segel and Jackson (1972). In other contexts, interesting spatial aggregation patterns can emerge when a cell population responds to gradients in some chemical signal. Together with E.F. Keller, Lee Segel in Keller and Segel (1971) and Keller and Segel (1970) proposed and gave a partial analysis of the first mathematical model of such chemo-sensitive spatial aggregation for a species of cellular slime mold. In terms of the cell population u, the chemical concentration v, and the chemotactic sensitivity χ, the resulting general chemotaxis model pioneered by Keller and Segel has the form

$$u_t = D_u \Delta u - \nabla \cdot [u\chi(u, v)\nabla v] + f(u, v)\,, \qquad v_t = D_v \Delta v + g(u, v)\,. \tag{2}$$

The classical Keller–Segel model corresponds to the special choice $\chi = 1$, $f = 0$, and $g = -v + u$ in (2).

In contrast to the survey of Maini et al. (1997), this review does not discuss the critically important issue of the modeling of biological or chemical phenomena by RD systems, nor does it survey the more mathematically abstract results relating to a rigorous mathematical analyses of RD patterns. This survey only focuses on pattern formation for continuum models, and does not discuss important recent analytical approaches for the systematic derivation of partial differential equation pattern-forming models by taking continuum limits of microscopic discrete random-walk models. The pivotal role of the development and refinement of mathematical models for the study of phenomena in the natural sciences is emphasized in the classic text of Lin and Segel (1974).

For nonlinear differential equation models in biology, fluid mechanics, and other areas, a key preliminary step in the analysis of a model is to introduce dimensionless variables in order to extract dimensionless parameters that characterize the behavior of the system. The central importance of identifying dimensionless parameters in a model was emphasized by Lee Segel in Segel (1972). When some of these dimensionless parameters take on extreme values, the original model can often be reduced to a simpler model that is easier to analyze. In the 1960s and early 1970s there was an intense focus on developing asymptotic methods to simplify differential equation models in the limit of extreme values of dimensionless parameters. One such method, called the method of multiple scales, applies to wave-type problems where there are two time scales; a fast oscillation together with a slow modulation of the envelope of the fast oscillation. This method allows for an accurate solution over asymptotically long time intervals. For other problems involving disparate spatial scales, the method of matched asymptotic expansions provides for the resolution of boundary layers and other localized spatial regions where the solution changes rapidly. The importance of such asymptotic methods as a way of systematically reducing intricate mathematical models into a form more amenable to analysis was emphasized by Segel in Segel (1966), and in his later paper Segel and Slemrod (1989) on quasi-steady state analysis. Many formal asymptotic methods are described and applied in Kevorkian and Cole (1981).

Starting in the late 1960s there was an increased focus on the development of a "bifurcation theory" to describe the branching behavior of solutions to differential equations as a function of dimensionless parameters, and to determine mathematical principles governing the exchange of stability of intersecting solution branches. Key rigorous results in this theory are given in Crandall and Rabinowitz (1973) and Chow and Hale (1982). In the early 1970s, an important formal asymptotic technique based on the method of multiple scales and the Fredholm alternative, was introduced in Matkowsky (1970) and Habetler and Matkowsky (1975) to study the exchange of stability of bifurcating solution branches in a sufficiently small neighborhood of a transcritical bifurcation point for a scalar RD model. Beginning in the early 1970s, related types of weakly nonlinear theories were developed to treat a wide range of problems in mathematical biology and hydrodynamic stability. For the RD system (1) there were many studies devoted to characterizing small-scale instabilities of spatially homogeneous equilibrium solutions near bifurcation points for various choices of the kinetics in (1). These studies for (1) are divided into two main groups; the finite-domain problem with suitable homogeneous boundary conditions, and the spatially extended model where (1) is posed in all of $\mathbb{R}^N$.

For the finite-domain problem, a Turing instability is determined by first linearizing (1) around a spatially homogeneous equilibrium solution and then examining the behavior of discrete spatial Fourier modes as a function of a dimensionless bifurcation parameter λ in the kinetics in (1). Weakly nonlinear theory for a Turing instability corresponds to studying the temporal evolution of the small $O(\varepsilon)$ amplitudes of any unstable Fourier modes within a small $O(\varepsilon)$ neighborhood of the neutrally stable bifurcation point $\lambda = \lambda_c$. The derivation of these amplitude equations, which evolve over an asymptotically long time interval, is based on a formal multiple-scale method similar to that of Matkowsky (1970) for the one-component system. The analysis incorporates projections of the nonlinear term f on the discrete unstable Fourier modes in a perturbative way. The resulting amplitude equations encode the stability properties of the bifurcating solution branch. In two spatial dimensions, this type of analysis can be used to derive amplitude equations for small amplitude stripe solutions and hexagonal structures. For (1) in a two-dimensional domain, the prediction of stripes versus spots, based on either cubic or quadratic terms in the expansion of the kinetic terms in (1) around a homogeneous base state, was given in Ermentrout (1991). Early examples of this type of analysis include Keener (1976) for the Brusselator model and Keener (1978) for an activator–inhibitor system. Many other studies for (1) and related finite-domain problems can be found in Murray (2003), Nicolis and Prigogine (1977), Grindrod (1996), and in Chapter 6 of Britton (1986).

For (1) on an infinite domain, a Fourier transform analysis readily shows that the instability of a spatially homogeneous equilibrium solution near a bifurcation point results from a continuous band of unstable modes, instead of discrete modes as for the finite-domain problem. For the infinite-domain problem, the resulting amplitude equation characterizing a weakly nonlinear instability near a bifurcation point is a partial differential equation that evolves over long time and space scales, and that has a diffusive scaling law. As an example, consider (1) in one spatial dimension and suppose that the linearization of (1) around a spatial homogeneous equilibrium solution has a Hopf bifurcation at some critical value $\lambda = \lambda_c$ of a control parameter in the kinetics of (1). Then, for $\lambda - \lambda_c = O(\varepsilon)$, and with $X = O(\varepsilon)x$ and $T = O(\varepsilon^2)t$, a multiple-scale analysis leads to the complex Ginzburg–Landau (CGL) amplitude equation

$$\mathbf{A}_T = \mu\mathbf{A} - (1 + i\alpha)|\mathbf{A}|^2\mathbf{A} + \gamma(1 + i\beta)\mathbf{A}_{XX}, \tag{3}$$

where the real constants α, β, γ, and μ, are determined by the kinetics and diffusivities in (1). This CGL provides a universal description of pattern formation in RD systems near a Hopf bifurcation point. The real-valued Ginzburg–Landau equation, where $\alpha = \beta = 0$ in (3), is the amplitude equation near a Turing instability. The CGL has no variational structure and, as such, admits a rich variety of solutions including spiral waves, pulses, traveling waves, etc. An excellent introduction to the CGL is given in Saarloos (1994). Weakly nonlinear theory for RD systems is discussed at length in Borckmans et al. (1995) and for the Brusselator model in Chapter 14.3 of Walgraef (1997).

For other spatially extended systems, such as those arising in convection or hydrodynamic stability problems, weakly nonlinear theories have played a pivotal role in classifying solution behaviors near bifurcation points and for identifying and classifying secondary instabilities such as Eckhaus instabilities, zigzag instabilities, etc. A key feature in many of these studies is the systematic derivation of PDE amplitude equations for certain order parameters that govern the evolution of the system over long time and spatial scales near a bifurcation point. Although the CGL (3) is probably the most common such amplitude equation, there are many other such “normal form” equations that have been derived and studied. In particular, in the study of periodic structures in Bénard convection, the Newell–Whitehead–Segel amplitude equation governs the slow spatio-temporal evolution of the periodic structure near a bifurcation point. This equation was derived independently by Lee Segel in Segel (1969) and by Newell and Whitehead in Newell and Whitehead (1969). Comprehensive surveys and examples of weakly nonlinear theory for various physical and chemical systems are given in de Wit (1999), Cross and Hohenburg (1993), van Hecke et al. (1994), Nicolis and Prigogine (1977), and Walgraef (1997).

Other approaches to study pattern formation, based on dynamical systems and group theory, were initiated in the mid-1970s as alternatives to formal weakly nonlinear multi-scale analyses. For spatially extended systems, one focus of the symmetry-group approach was to characterize the form of the amplitude equation and the possible bifurcations in terms of the group symmetries of the underlying problem. The pivotal role of the "normal form," representing universal descriptions of the dynamics near bifurcation points, was emphasized in Golubitsky et al. (1988). In addition, for finite-domain problems, the development of center manifold theory (cf. Carr, 1981) allowed for the rigorous derivation of ODE amplitude equations near bifurcation points by systematically projecting the nonlinear terms onto the neutral subspace of the linearization, and then using the spectral gap between eigenvalues to control the error terms over long time intervals. At certain codimension-two bifurcations, such as at a simultaneous Turing/Hopf bifurcation where the ODE amplitude equations are three-dimensional, such a center manifold reduction was crucial for proving the existence of chaotic dynamics in the original PDE model for very narrow parameter regimes. A critical review of this behavior for the Brusselator model is given in Wittenberg and Holmes (1997).

Despite the success of "normal form" weakly nonlinear theory in describing small-amplitude pattern formation near bifurcation points, there are rather few general results for characterizing the stability and dynamics of spatially localized patterns that deviate substantially from a spatially uniform state. Different types of localized patterns, where singular perturbation analysis is essential, include interfacial patterns, localized pulses and spots, spatially aggregating solutions in chemotaxis, spiral waves in excitable media, and singular or blow-up solutions to PDEs. Starting in the mid-1980s, and continuing to date, there has been an increased focus on examining the stability and dynamics of such localized solutions. In his pioneering numerical study for the Gray–Scott RD model in 1993, (Pearson, 1993) computed a variety of interesting finite-amplitude patterns in different parameter regimes that involve either localized stripes, labyrinths, oscillating spots, or self-replicating spots. Many of these patterns are remarkably similar to those observed in the experimental studies of Lee and Swinney (1995) and Lee et al. (1994). With regards to the intricacy of these patterns, and the ubiquity of weakly nonlinear analysis in the RD literature, Pearson Pearson (1993) commented that "It is unclear whether the patterns presented in this report will yield to these now-standard technologies." Further emphasizing this point, in his recent survey chapter on pattern formation, Knobloch (2003) remarks that "The question of stability of finite amplitude structures, be they periodic or localized, and their bifurcation is a major topic that requires new insights."

In general, the study of the stability and dynamics of localized patterns is reliant on establishing some global bifurcation properties of spatially localized finite-amplitude solutions. This is in contrast to weakly nonlinear theory that requires only local bifurcation properties of solution branches. The development of reliable numerical software over the past 30 years has allowed for careful numerical investigation of finite-amplitude pattern formation and global bifurcation properties. In the 1970s and 1980s, analytical methodologies from the maturing field of bifurcation theory were incorporated into sophisticated numerical algorithms to numerically compute solution branches for both ODE and PDE problems. Algorithms for the accurate detection of saddle-node, transcritical, Hopf, and higher codimension, bifurcation points were devised. In addition, path-following algorithms and branch-switching strategies were developed for computing multi-valued solution branches. Pioneering analytical results and numerical algorithms for treating bifurcation problems are given in the monograph Keller (1987). Based on this theory, a general-purpose bifurcation software for ODE systems, called AUTO (cf. Doedel and Wang, 1994), was in common use in the late 1980s. Recent extensions of this ODE software, which are based on further analytical advances in bifurcation theory, include techniques for path-following homoclinic orbits in ODE systems (cf. Champneys et al., 1996). The software package XPPAUT (cf. Ermentrout, 2002), which provides a flexible user interface to the basic AUTO routines, is popular with researchers and students in a wide variety of disciplines. A comprehensive overview of numerical bifurcation algorithms, as well as methods for the automatic computation of normal forms, is given in Beyn et al. (2002) and Doedel and Tuckerman (2000). For elliptic PDEs, global bifurcation and stability behavior of multi-valued solution branches is accurately computed using the software package PLTMG (cf. Bank, 1998), which combines adaptive finite-elements, path following-strategies, and the accurate detection of bifurcation points. In addition, over the past 10 years, sophisticated numerical software such as moving-mesh methods have been developed to compute time-dependent thin-interface patterns and near-singular behavior in PDE models. These methods have been used in Budd et al. (2005) and Ren and Wang (2000) to compute near blow-up behavior for the classical Keller–Segel model of chemotaxis. More recently, sophisticated PDE software based on adaptive finite elements has been developed in Madzvamuse et al. (2005) and Madzvamuse et al. (2003) for numerically studying pattern formation in RD systems on growing domains.

We will now describe a few important classes of localized solutions for RD systems. We begin with blow-up solutions to PDEs. In the PDE community, there were some conjectures made in the 1970s regarding the occurrence of finite-time singularities for certain PDE models. In particular, the formal studies of Nanjundiah (1973) and Childress and Percus (1981) suggested that solutions to the classical Keller–Segel model, obtained by setting $\chi = 1,\ f = 0$, and $g = -v + u$ in (2), can exhibit infinite aggregation at finite time in three space dimensions, and in two space dimensions for sufficiently large total mass. Motivated by this chemotaxis problem, and by combustion problems with exponential nonlinearities where blow-up behavior was anticipated, a systematic mathematical theory for establishing the existence of finite-time singularities was initiated in the 1980s. In the simpler context of studying blow-up behavior in the scalar PDE $u_t = \Delta u + u^p$ for $p > 1$, an important step was made in Filippas and Kohn (1992) where center manifold theory and a quasi-similarity solution were used to give a rigorous construction of the solution near the point and time of blow-up. By using a related approach, it was only in 1996 in Herrero and Velázquez (1996) that a rigorous construction of the local blow-up profile was made for the Keller–Segel model in two space dimensions. An attempt to regularize the Keller–Segel model to generate large, but finite, amplitude aggregation patches is given in the recent paper Velazquez (2004). The mathematical technology for the analysis of blow-up solutions to chemotaxis and other PDE models is now rather well developed. A comprehensive survey of the literature on chemotactic blow-up is given in Horstmann (2003).

Another type of localization phenomenon in RD systems concerns patterns with thin interfaces that separate two states of the system. For example, such patterns can occur for (1) in the limit of small diffusivities when the nonlinear terms in (1) are of bistable type. The asymptotic analysis of thin-interface patterns, pioneered by Fife (1988) and the Japanese school of researchers in RD systems (see the monograph by Nishiura (2002) and the references therein), relies on the method of matched asymptotic expansions, also commonly referred to as singular-limit analyses. The simplest setting for the study of thin-interface patterns is for PDEs that admit a gradient-flow variational formulation in terms of some energy functional. Such variational problems are common in the field of materials science where patterns are formed through a balance of bulk and interfacial energies. Two problems of this type are the Allen–Cahn and Cahn–Hilliard (cf. Cahn and Hilliard, 1958) systems given by

$$
\begin{aligned}
u_t &= \varepsilon^2 \Delta u - V_u(u), \quad \text{(Allen–Cahn)};\\
u_t &= \Delta \left(-\varepsilon^2 \Delta u + V_u(u)\right), \quad \text{(Cahn–Hilliard)}, \qquad (4)
\end{aligned}
$$

where $V(u)$ is a symmetric double-well potential, such as $V(u) = (1 - u^2)^2$. In mathematical biology, the Cahn–Hilliard equation also arises in the study of long-range diffusion of a nondilute population with density $u(x, t)$, where Fick's law, representing a diffusive flux proportional to the density gradient, is not appropriate. In this context, in Novick-Cohen and Segel (1984) Lee Segel, together with his student Amy Novick-Cohen, gave one of the first analyses to construct finite-amplitude equilibrium solutions to the Cahn–Hilliard model in one space dimension. In one space dimension, the evolution of a collection of interfaces for the Allen–Cahn and Cahn–Hilliard models is distinctly different from that in higher space dimensions. In the one-dimensional case, the motion of interfaces for $\varepsilon \to 0$ is asymptotically exponentially slow with respect to the thickness ε of the interface. This phenomenon, known as dynamic metastability, was studied in Alikakos et al. (1991), Carr and Pego (1989), Fusco and Hale (1989), and is surveyed in Ward (1998).

For the Allen–Cahn PDE of (4) in N space dimensions, a pioneering use of the singular-limit analysis was made in Rubinstein et al. (1989). For $\varepsilon \to 0$ and for $t \gg 1$, it was shown in Rubinstein et al. (1989) that the solution to the Allen–Cahn equation reduces to $u \sim \pm 1$ on either side of an interface Γ, whose normal velocity V is related to the mean curvature κ of Γ by $V = \varepsilon^2 \kappa$. For the fourth-order Cahn–Hilliard model, a related formal singular-limit analysis was made in Pego (1989). For $\varepsilon \to 0$ and on a slow time-scale, it was shown in Pego (1989) that the normal velocity of the interface Γ depends on the jump across the interface of the normal derivative of a function which is harmonic on either side of the interface, and which equals the mean curvature on the interface. This limiting problem characterizing interface propagation is very closely related to the quasi-static two-phase Stefan model of solidification, known as the Mullins–Sekerka problem. A rigorous analysis of the formal singular-limit analysis of Pego (1989) is given in Alikakos et al. (1994). Although the transient dynamics of pattern formation in gradient-flow systems can be rather complicated, the ultimate steady-state configuration based on the minimization of an energy functional, with a possible side constraint such as mass conservation, is rather simple. A survey of results for interface propagation in the fourth-order Cahn–Hilliard model and its extensions is given by Novick–Cohen in Novick-Cohen (1998). A comprehensive review of interfacial behavior in gradient-flow systems is given in Fife (2002). Recent results on spatial pattern formation in more general fourth-order scalar models are found in Peletier and Troy (2001). The fourth-order Cahn–Hilliard model can be heuristically derived from a truncated moment expansion of a partial-integro-differential convolution-type model of nonlocal diffusion. Fully nonlocal diffusion models have been analyzed recently in Bressloff (2005) and Liang and Troy (2003) in the study of spatial patterning of neuroactivity, and in Mogilner et al. (1996) and Mogilner and Edelstein-Keshet (1996) in the study of swarming behavior of insects and other social organisms.

In contrast to the well-studied gradient-flow problems, there are relatively few general results for the existence, stability, and dynamics of thin interfaces for nonvariational RD systems. In one spatial dimension, an important technique, called the Singular Limit Eigenvalue Problem (SLEP) method, was introduced in Nishiura and Fujii (1987) for determining the linearized stability of equilibrium internal-layer solutions to a generalized Fitzhugh–Nagumo model in one space dimension. Similar SLEP-type methods, as surveyed in Section 5.4 of Nishiura (2002), can be applied to interfacial patterns in other problems for calculating eigenvalues that tend to zero with the thickness of the interface. This method was used in Taniguchi and Nishiura (1994) to study the stability of a planar interface to transverse perturbations for a generalized Fitzhugh–Nagumo model. In two or more space dimensions, singular-limit analyses for nonvariational RD systems typically lead to sharp interface free-boundary problems, where the evolution of the interface is determined in terms of its mean curvature. These free-boundary problems are often very closely related to the traditional, but notoriously difficult, Stefan free-boundary problems that are common in solidification theory. Examples of such studies include Sakamoto (1998) and Goldstein et al. (1996) for generalized Fitzhugh–Nagumo models, and Dancer et al. (1999) for a two-species diffusive competition model in the spatial segregation limit.

Interfacial patterns can also occur for generalized chemotactic aggregation systems of the form (2) in the singular limit of a small diffusivity for either u or v. In one spatial dimension, it was shown in Dolak and Schmeiser (2006) and Potapov and Hillen (2005) that the spatial regions of aggregation in the singularly perturbed volume-filling chemotaxis model, corresponding to setting $g = -v + u$, $f = 0$, $D_u = \varepsilon^2 \ll 1$, $D_v = 1$, and $\chi = (1 - u)$ in (2), can exhibit metastable behavior as $\varepsilon \to 0$ similar to that of the Cahn–Hilliard model. In two-space dimensions, the numerically computed interfacial patterns shown in Fig. 10 of Painter and Hillen (2002) also bear a striking resemblance to those found for the Cahn–Hilliard model. For a generalized chemotaxis model with growth, where $f \neq 0$ in (2), it was shown in Bonami et al. (2001) that the motion of the interface bounding the region of aggregation depends on the mean curvature of the interface and on a nonlocal term. For a different generalized chemotaxis model incorporating growth effects, instabilities of interfacial ring-type patterns leading to spot formation have been computed numerically in Woodward et al. (1995). Results for other generalized chemotaxis models are surveyed in Horstmann (2003). For a survey of singular-limit processes for nonvariational RD and generalized chemotaxis models see Mimura (2003) and Chapter 5 of Nishiura (2002) (and the references therein). There are many open problems in this area that await a systematic analytical investigation.

In contrast to interfacial patterns, other classes of singularly perturbed RD systems allow for localized patterns in the form of spikes or pulses in one-space dimension, and spots in higher space dimensions. This type of pattern localization to certain points in the domain is common in activator–inhibitor models, such as the classic Gierer–Meinhardt (GM) model, and in substrate-depletion models, such as the Gray–Scott (GS) model. For (1) with the GM kinetics $f = -u + u^2/v$ and $g = -v + u^2$, and with $D_v \gg 1$ and $D_u = \varepsilon^2 \ll 1$ in (1), the profile for the activator concentration u in the vicinity of a spot in dimension N is proportional to dilations of the unique radially symmetric solution $w(\rho)$ satisfying

$$w'' + \frac{(N-1)}{\rho} w' - w + w^2 = 0\,, \quad \rho \geq 0\,;$$
$$w(0) > 0\,, \quad w'(0) = 0\,, \quad w(\infty) = 0\,. \tag{5}$$

In one space dimension, where $N = 1$, the pulse profile for the activator is $w(\rho) = \frac{3}{2}\text{sech}^2(\rho/2)$. Motivated largely by the review article (Ni, 1998) on spikes, there are now many results for the existence, stability, and dynamics of spike and spot patterns to the GM model. In one space dimension, the existence and stability of equilibrium spike patterns for the GM model have been studied for the regime $D_u = O(\varepsilon^2)$ and $D_v = O(1)$ in Iron et al. (2001), Ward and Wei (2003), and Doelman et al. (2001). Through the analysis of certain nonlocal eigenvalue problems, instabilities of spike patterns are shown to result from one of two possible mechanisms; an overcrowding instability for closely spaced spikes, and an oscillatory instability in the amplitudes of the spikes in the activator concentration u when the inhibitor v responds sufficiently sluggishly to small changes in u (cf. Ward and Wei, 2003). Similar oscillatory and overcrowding instabilities of spikes can occur for the GS model (cf. Doelman et al., 1998; Muratov and Osipov, 2002; Kolokolnikov et al., 2005a). Stability results for spots in the GM model in two space dimensions are given in Wei and Winter (2001). For various RD systems, results for the dynamics of pulses and spots are given in Ei (2002), Kolokolnikov and Ward (2003), and Sun et al. (2005), and pulse–pulse collision events are studied in Nishiura et al. (2003) in terms of global bifurcation properties.

An interesting feature of pulse and spot patterns for the GM and GS models is that these patterns can undergo pulse- or spot-splitting events in certain parameter regimes. Therefore, starting from a localized seed initial data, many pulses or spots can be generated as time increases. Such self-replication behavior cannot occur in gradient-flow systems that are governed by the decrease in some energy functional. A self-replication behavior, whereby only the edge pulses or spots undergo splitting events, was first observed numerically for the GS model in Pearson (1993) and Nishiura and Ueyama (1999) for the parameter regime where both diffusivities D_u and D_v in (1) are asymptotically small. In Nishiura and Ueyama (1999) a theoretical explanation for this behavior was given in terms of certain global bifurcation properties of equilibrium solution branches to the GS model, which can be verified using the bifurcation software AUTO Doedel and Wang (1994). Global bifurcation properties were also critical to the study of Nishiura and Ueyama (2001) for determining a parameter range in the GS model where both self-replication and spot-annihilation phenomena can occur simultaneously. The resulting spot patterns in Nishiura and Ueyama (2001) were found to exhibit spatio-temporal chaos. More generally, for other singularly perturbed RD models, global bifurcation conditions thought to be essential for an edge-splitting self-replication behavior were formulated in Ei et al. (2001). Edge-splitting pulse-replication behavior can also occur for the GM model (cf. Doelman and van der Ploeg, 2002), and a simultaneous pulse-splitting behavior occurs for the GS model in the parameter range where the diffusivity ratio D_u/D_v is sufficiently small (cf. Doelman et al., 1998; Muratov and Osipov, 2000; Kolokolnikov et al., 2005b). A review of spike behavior in RD systems, with a list of open problems, is given in Ward (2005).

A new recent focus in RD theory concerns the numerical computation and analysis of pattern formation on domains that are growing in time. A key conclusion, as obtained in Crampin et al. (1999), is that the domain growth can significantly enhance the reliability of pattern selection, such as the formation and self-replication of stripes, without tight control of parameter values in the reaction kinetics. This feature has important consequences in the modeling of biological morphogenesis. For a RD system with certain piecewise-linear kinetics in an exponentially growing one-dimensional domain with small growth rate, spatial transitions in pattern formation resulting from either peak-splitting or peak insertion have been analyzed in Crampin et al. (2002) in the large diffusivity ratio limit. Numerical studies of pattern formation on growing one- and two-dimensional domains are given in Madzvamuse et al. (2005) and Madzvamuse et al. (2003). In addition, a generalized chemotaxis-reaction-diffusion system on a slowly growing domain has been proposed and studied numerically in Painter et al. (1999) as a model for stripe insertion on the skin of a species of juvenile angelfish (cf. Kondo and Asai, 1995). For RD problems on domains that are slowly growing, an interesting open problem is to perform a rigorous quasi-steady analysis of pattern formation, punctuated by rapid pattern transitions, for general forms of the reaction kinetics.

In parallel to the advances of singular-limit analyses for RD systems based on the method of matched asymptotic expansions, over the past 10 years there have been important breakthroughs in dynamical systems methodologies for the analysis of finite-amplitude patterns for, essentially, one-dimensional spatially extended systems. Such patterns include pulses, wavetrains, viscous shocks and other internal layers, and Archimedean spiral-wave solutions. A comprehensive survey of these developments is given in Fiedler and Scheel (2003). One cornerstone in this theory is the "Geometric Theory of Singular Perturbations," as surveyed in Jones (1994), which often leads to rigorous constructions of localized equilibrium solutions to RD systems by analyzing intersections of slow–fast solution manifolds for singularly perturbed ODE systems. In this theory, asymptotic matching is viewed as a geometric transversality condition between solution manifolds. A second cornerstone in this approach is the development of a detailed spectral theory, which emphasizes the Evans function and the critical role of the absolute and essential spectrum, for analyzing the linearized stability of these solutions (cf. Sandstede, 2002; Fiedler and Scheel, 2003; Rademacher et al., 2005). A notable success of this theory concerns a detailed stability analysis of rotating spiral-wave solutions to singularly perturbed excitable RD systems, including the Fitzhugh–Nagumo model on unbounded or very large domains. An asymptotic construction of a spiral wave, as described in Fife (1988), Tyson and Keener (1989), Barkley (1992), Margerit and Barkley (2002), and Section 4.3 of Nishiura (2002), involves a delicate asymptotic matching between the spiral core and its far-field, which then leads to a nonlinear eigenvalue problem for the spiral rotation frequency. Spiral wave phenomena in various biological and chemical contexts is surveyed in Winfree (1991).

Recent theoretical advances have led to the analysis of several distinct modes of spiral instability; a meandering or oscillatory instability of the tip of the spiral due to a subcritical Hopf bifurcation (cf. Barkley, 1992; Sandstede et al., 1999; Fiedler and Scheel, 2003), and a breakup of the spiral core or its far-field due to either point eigenvalues or essential spectra that penetrate into the unstable right half-plane (cf. Sandstede and Scheel, 2000b; Wheeler and Barkley, 2006). On a large bounded domain, the possibility of a de-stabilization of the spiral core is closely related to the problem of locating what is known as the "absolute spectrum" of the infinite-domain problem (cf. Sandstede and Scheel, 2000a,b; Wheeler and Barkley, 2006). The advances in spectral theory have also led to important theoretical developments in other contexts, including a comprehensive study of convective and absolute instabilities of traveling-wave solutions of RD systems (cf. Sandstede, 2002). In addition, there is now a rather mature theory for the problem of wave-speed selection for traveling fronts in a bistable RD equation (cf. Saarloos, 2003).

In this brief historical survey we have illustrated the important role that Lee Segel had in the development of analytical approaches for the study of pattern formation in reaction-diffusion and related systems. I hope that this survey and bibliography will stimulate students and other researchers to make further contributions to this exciting field.

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