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Transient and steady state of mass-conserved reaction-diffusion systems

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Reaction-diffusion systems with mass conservation are studied. In such systems, abrupt decays of stripes follow quasistationary states in sequence generally. We give a stability condition of steady state which the system reaches after long transient time. It is also shown that there exist systems in which a single-stripe pattern is solely steady state for an arbitrary size of the systems. The applicability to cell biology is discussed.

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Pattern formation, the emergence of a spatial structure from an initially uniform state, has often been studied on the framework of reaction-diffusion systems (RDS). It is extensively applied to physical, chemical, and biological systems to explain their specific spatial structures [1,2]. Turing instability is the most prominent mechanism, forming spatially periodic stripes [3]. The intrinsic distance between stripes is, in principle, estimated by the linear stability analysis at a homogeneous state [1–3]. However, this estimation could be invalid when applied far from a uniform state. For example, a second bifurcation can arise which would indicate the collapse of a simple periodic structure [4]. In such situations, the transient dynamics of pattern formation would be difficult to predict. In general, RDS shows various dynamics even when steady states are reached [5]. So far, a few studies have discussed transient dynamics using the computational analysis of the famous Gray-Scott model [5,6] and by reduced dynamics on the slow manifold [7–9].

In this paper, we study a class of RDS in the context of the above aspects. We consider RDS showing instability at uniform state, in which no production and no degradation of substances occur [10,11]. Such situations often arise in the biological models, particularly at the scale of cells (see later discussion) [12,13]. As we will see, the following properties are commonly observed in such RDS; (i) the transient dynamics is a sequential transition among quasisteady states, with a decrease in the number of stripes. (ii) The distance between resultant stripes cannot be estimated from the linear analysis at uniform state. In particular, there are systems in which a one-stripe pattern is a solely stable state regardless of the system size.

Consider a diffusible chemical component with two internal states, U and V. Diffusion coefficients are D_u and D_v, respectively, for which we can set $D_u < D_v$ without loss of generality. The transition rates between U and V are regulated by each other. We studied a one-dimensional system with size $L (0 \le x \le L)$ under periodic boundary conditions unless otherwise stated. Concentrations in U and V at position x and at time t are represented by $u(x,t)$ and $v(x,t)$, respectively, and obey the following equations:

$$\partial_t u = D_u \partial_x^2 u - f(u,v), \tag{1}$$

$$\partial_t v = D_v \partial_x^2 v + f(u,v). \tag{2}$$

Obviously, the total quantity of the substances (total mass) is conserved,

$$s = \frac{1}{L}\int_0^L (u+v)dx, \tag{3}$$

s is the average concentration of the substance, which is determined by the initial condition $u(x,0)$ and $v(x,0)$.

Below, all numerical simulations were performed with $f(u,v) = au/(b+u^2) - v$ where $s=2.0$, $a=1.0$, $b=0.1$, $D_u=0.02$, and $D_v=1.0$. We observed qualitatively the same phenomena in several mass-conserved models [13].

Uniform state $\vec{w}^* = (u^*, v^*)$ is derived from the following conditions; $u^* + v^* = s$ and $f(u^*, v^*) = 0$ (stable fixed point in kinetic equation). Let f_u^* (f_v^*) be partial derivatives of f with regard to u (v) at $\vec{w}^*$. If the following relations are satisfied, uniform state $\vec{w}^*$ loses its stability in Turing-like manner [19], and the pattern starts to rise,

$$f_v^* < f_u^* < 0, \tag{4}$$

$$D_u f_v^* - D_v f_u^* > 0. \tag{5}$$

All the waves (e^{ikx}) with wave number k between $0 < k^2 < (D_u f_v^* - D_v f_u^*)/D_u D_v$ are unstable.

At the beginning of the dynamics, the wave with the largest instability grows (see A in Fig. 1, and the line segment representing the most unstable wavelength ℓ_m). In a mass-conserved system, characteristic transient processes are observed. After the growth of a number of stripes (A in Fig. 1), some stripes stop growing and begin to decay (B). With the decay of a stripe, neighboring stripes grow due to mass conservation. The distance between neighboring stripes becomes larger ($B-C$). If the distance is large enough the state appears to reach a steady state (C, quasisteady state). However, one (or more) stripe(s) collapses abruptly with the concomitant growth of adjacent stripes (D). As the process continues, the number of stripes decreases and the intervals between the abrupt transitions gets longer (notice the log-scale representation in Fig. 1). In Fig. 1, the system finally reaches a one-peak state. The wavelength is much larger than ℓ_m. Similar processes were observed in many mass-conserved systems.

To understand the observed transient processes, consider the stationary patterns of the system with size L. A stationary

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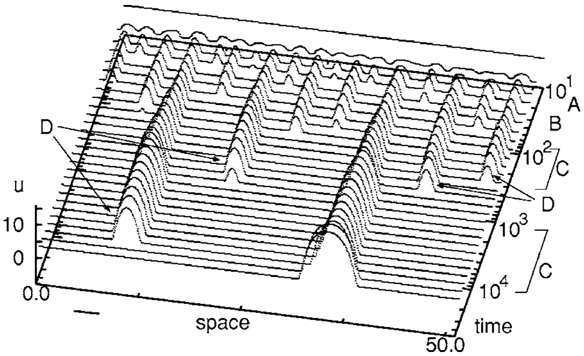

FIG. 1. Transient dynamics of a mass-conserved system. The model system and the meaning of alphabet letters are explained in the text. System size was chosen as $L=50.0$ here. Note that time scale is represented by log scale. In the system, the most unstable wavelength at homogeneous state is $\ell_m=3.2$, shown by the line segment in the left bottom. We checked that the system eventually falls to a one-stripe pattern for any system size between $2.0\leq L\leq 100.0$.

pattern $\vec{w}_0(x)=(u_0(x),v_0(x))$ is given by the solution of Eq. (1) and (2) with left-hand sides replaced by 0. In a mass-conserved system, there is a family of stationary solutions parametrized by s, represented by $\vec{w}_0(x;s)$ explicitly. A function $h(x)$ and a value P exist, such that $u_0=h(x)/D_u$ and $v_0(x)=[-h(x)+P]/D_v$, and satisfy the following equations:

$$P=D_u u_0(x)+D_v v_0(x), \tag{6}$$

$$\frac{d^2h(x)}{dx^2}=f\left(\frac{h}{D_u},\frac{-h+P}{D_v}\right). \tag{7}$$

Notice $D_u u_0(x)+D_v v_0(x)$ is independent of x. P is related to s by $P=D_v s-(D_v-D_u)\bar{h}/D_u$, in which $\bar{h}=\frac{1}{L}\int_0^L h(x)dx$ is the average of $h(x)$.

Let us represent the linear operator at a stationary state $\vec{w}_0$ by $\mathcal{L}$. There are two eigenfunctions belonging to the zero eigenvalue (0-eigenfunctions); $\partial_x\vec{w}_0=(\partial_x u_0,\partial_x v_0)$ and $\partial_s\vec{w}_0=(\partial_s u_0,\partial_s v_0)$. The former function is derived from the fact that the arbitrary translation of stationary state, $\vec{w}_0(x+\Lambda)$ is also stationary, while the latter is from the conservation property of the mass. Adopting usual L^2-inner product, $\vec{\phi}=(1,1)$ is the conjugate vector of $\partial_s\vec{w}_0$ because $\langle\vec{\phi},\partial_s\vec{w}_0\rangle_L=1$ and $\langle\vec{\phi},\partial_x\vec{w}_0\rangle_L=0$.

Now, to evaluate the stability of a stationary pattern, consider the two peak situation. Take the one-stripe stationary state $\vec{w}_0$ in the system with $\frac{L}{2}$ length, which takes the minimum u_0 at $x=0(=\frac{L}{2})$ and the maximum at $x=\frac{L}{4}$. Then copy the exact same state on $\frac{L}{2}<x<L$, and name the system on $0\leq x\leq L$ as the unperturbed system (UPS). Left and right halves are independent of each other. Next, the boundary condition in UPS is changed at $x=0(=\frac{L}{2})$ and $\frac{L}{2}(=L)$ into the usual periodic boundary condition of the system on $0\leq x\leq L$. We refer to this modified system, which is the one we are interested in, as the perturbed system (PS). We represent the state constructed as above by $\vec{w}_0\oplus\vec{w}_0$, where the left- (right-) hand side of $\oplus$ represents the function on $0<x<\frac{L}{2}$ $(\frac{L}{2}<x<L)$. This state is obviously a stationary solution in both UPS and PS.

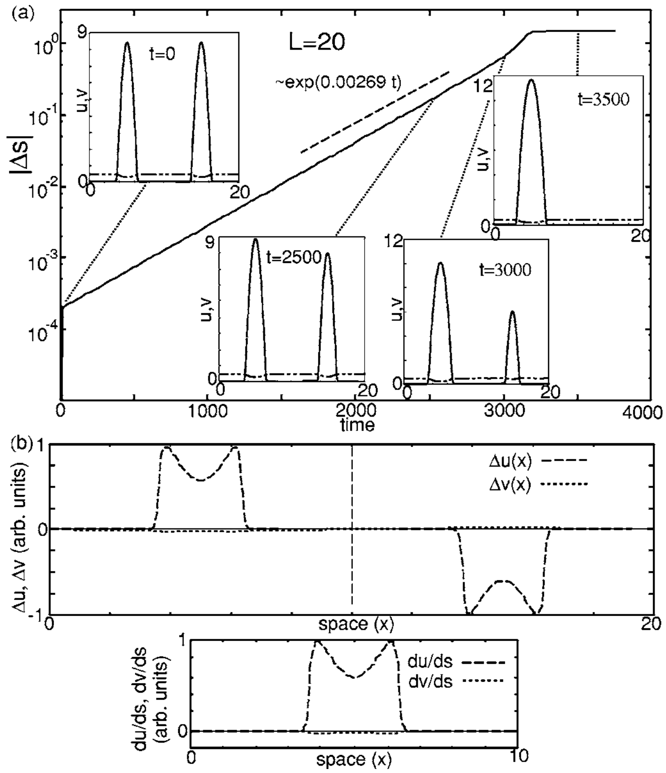

FIG. 2. Two identical steady solutions for $\frac{L}{2}=10.0$ are connected and perturbed (±1.0%, keeping total mass quantity) at $t=0$. (a) $|\Delta s|$ grows exponentially with time, indicating that one stripe decays while the other grows. $u(x,t)$ (solidline) and $v(x,t)$ (dashedline) at $t=0$, 2500, 3000, and 3500 are shown in insets. (b) $\Delta\vec{w}(x)$, the difference of $\vec{w}(x,t)$ between $t=200$ and 300 is shown in the top panel, while $\partial_s\vec{w}_0$ is shown in the bottom panel (normalization is applied).

Linear operators at the state are given by $\mathcal{L}_0$ for UPS and $\mathcal{L}$ for PS. Because UPS is simply the juxtaposition of identical systems, $\vec{\psi}_1^0=\partial_x\vec{w}_0\oplus\partial_x\vec{w}_0$ and $\vec{\psi}_2^0=\partial_s\vec{w}_0\oplus\partial_s\vec{w}_0$ are 0-eigenfunctions for $\mathcal{L}_0$. They are also 0-eigenfunctions in PS; $\mathcal{L}_0\vec{\psi}_i^0=\mathcal{L}\vec{\psi}_i^0=0$ $(i=1,2)$. Another 0-eigenfunction of $\mathcal{L}_0$ is $\vec{\psi}_3^0=\partial_s\vec{w}_0\oplus(-\partial_s\vec{w}_0)$ but this is not 0-eigenfunctions of $\mathcal{L}$ anymore [20]. However, when the amplitudes of $|\partial_s u_0|$ and $|\partial_s v_0|$ are small at $x=0$ and $\frac{L}{2}$, the discrepancy between UPS and PS is small and we can expect a function $\vec{\psi}=(\psi_u,\psi_v)$ and a value λ which are close to $\vec{\psi}_3^0$and 0, respectively, and that they satisfy the following relation:

$$\mathcal{L}\vec{\psi}=\lambda\vec{\psi}. \tag{8}$$

If λ is positive, then the stationary state $\vec{w}_0\oplus\vec{w}_0$ is unstable and small fluctuations grow as $\sim e^{\lambda t}\vec{\psi}$. Because $\vec{\psi}$ is similar to $\vec{\psi}_3^0=\partial_s\vec{w}_0\oplus(-\partial_s\vec{w}_0)$, the corresponding dynamics appears as the decay of a stripe and the growth of the other, as is observed in the numerical simulations. Note the conjugate function of $\vec{\psi}_3^0$ is $\vec{\phi}_L=\vec{\phi}\oplus(-\vec{\phi})$.

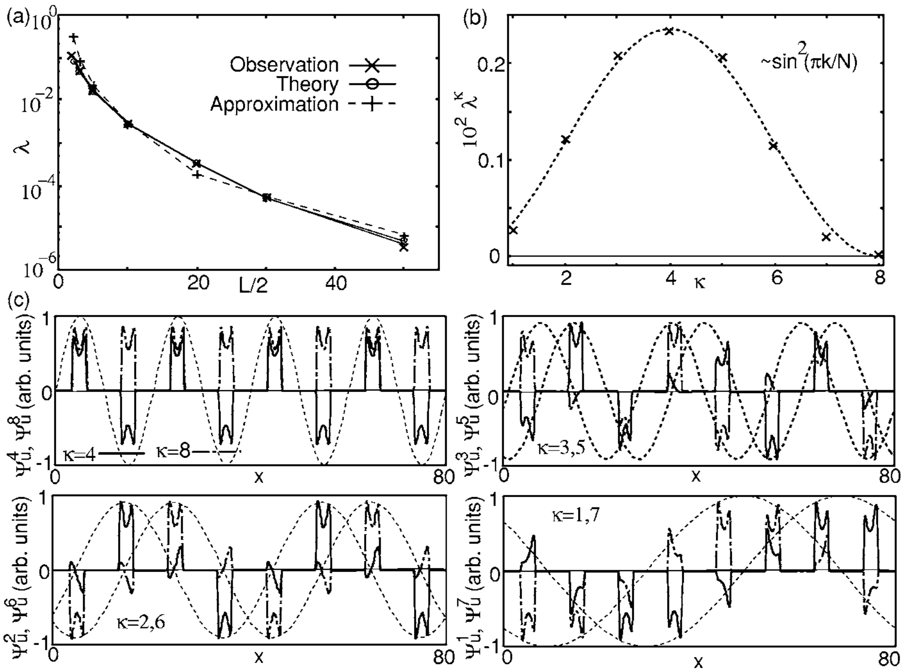

FIG. 3. (a) Growth rates λ for respective system sizes are evaluated from the observations of $|\Delta s(t)|$ (×) and from Eq. (9) (○). Approximated estimation of λ, $-\frac{4}{L^2}\partial_s P$, are also plotted (+). (b) Eigenvalues of $\mathcal{L}$ for the eight-stripe state are numerically calculated (L=80.0), and (c) corresponding eigenfunctions. Note that eigenvalues except κ=4,8 are degenerated. Sinusoidal curves are also shown for guidance.

To check the validity of the above considerations, we numerically measured some related quantities. At first, we simulated the equations in the $\frac{L}{2}$-length system and obtained a steady one-stripe state. Then, we extended the system size twice and copied the steady state to the region $\frac{L}{2}\leq x\leq L$. Next, perturbations were added keeping the total mass conserved and observed the resulting dynamics. $|\Delta s(t)| \equiv |\langle\vec{\phi}_L,\vec{w}\rangle_L| = \frac{1}{L}|\int_0^{L/2}(u+v)dx - \int_{L/2}^{L}(u+v)dx|$ is plotted in Fig. 2(a) which shows the exponential growth of the perturbation. Then, we compared $\vec{\psi}_3^0$ with the growing part of (u,v). In Fig. 2(b), $\Delta\vec{w}(x)=(\Delta u(x),\Delta v(x))$ is shown, where $\Delta\vec{w}(x) = \vec{w}(x,t_2)-\vec{w}(x,t_1)$ is the difference of $\vec{w}$ between two growing time points t_1 and t_2. $\Delta\vec{w}(x)$ is similar to $\vec{\psi}_3^0$ which validates the above considerations.

The expected $\vec{\psi}$ is a continuous and smooth function on $0\leq x\leq L$ and odd around $x=\frac{L}{2}$. Thus, it is enough to consider a nontrivial solution of Eq. (8) on $0\leq x\leq\frac{L}{2}$ with boundary condition $\vec{\psi}(0)=\vec{\psi}(\frac{L}{2})=0$. We can limit our arguments on $0\leq x\leq\frac{L}{2}$ in the following discussion. We properly redefine $\mathcal{L}$ under this limitation. To obtain $\vec{\psi}$ and λ in Eq. (8), $\vec{\psi}=\partial_s\vec{w}_0+\vec{\eta}$ is defined, where $\vec{\eta}$ is orthogonal to $\partial_s\vec{w}_0$ ($\langle\vec{\phi},\vec{\eta}\rangle_{L/2}=0$). In the first order of approximation, $\vec{\eta}$ satisfies the relation $\mathcal{L}\vec{\eta}=\lambda\partial_s\vec{w}_0$. Then we can obtain

$$\lambda = \left(\frac{D_v - D_u}{D_u D_v}\bar{A} + \frac{1}{D_v}\bar{\hat{Q}}\right)^{-1}, \tag{9}$$

where $\bar{A}=\frac{1}{L/2}\int_0^{L/2}A(x)dx$ and $\bar{\hat{Q}}=\frac{1}{L/2}\int_0^{L/2}\hat{Q}(x)dx$. Here $\hat{Q}(x)$ is defined as $Q(x)\equiv D_u\psi_u(x)+D_v\psi_v(x)=\lambda\hat{Q}(x)$, and is explicitly given by

$$\hat{Q}(x) = \int_0^x dx' \int_0^{x'} dx''[\partial_s u_0(x'') + \partial_s v_0(x'')] - \frac{L}{4}x, \tag{10}$$

and $A(x)$ is the solution of the following equation:

$$\frac{d^2A}{dx^2} - \left(\frac{f_u}{D_u} - \frac{f_v}{D_v}\right)A = \frac{f_v}{D_v}\hat{Q}(x) + \partial_s u_0 \tag{11}$$

with the boundary condition $A(0)=A(\frac{L}{2})=0$.

We calculated Eq. (9) numerically. Observed growth rates and estimated values from Eq. (9) are plotted in Fig. 3(a) against one-half of the system size $\frac{L}{2}$, which is the distance between two stripes. The two plots are in good agreement with each other and support the validity of the arguments presented.

From $Q(x)=\lambda\hat{Q}(x)$, we can obtain $\lambda=-\frac{4}{L}\frac{dQ(0)}{dx}$. In UPS, $Q(x)$ is given by $\partial_s P\oplus(-\partial_s P)$ and independent of x, while in PS $Q(x)$ is connected with 0 at x=0 and $=\frac{L}{2}$ by the modification of boundary conditions. Thus, the sign of $\frac{dQ(0)}{dx}$ is the same as $\partial_s P$ and the sign of λ is the opposite of $\partial_s P$. This leads to the condition of two stripe instability in the L-length system as

$$\partial_s P < 0. \tag{12}$$

This instability condition is true for any stationary state as seen below, and thus gives the criterion of the final state of mass-conserved RDS.

The above arguments with the two-stripes situation are extensible to an identical N-stripe pattern, where each stripe has $\frac{L}{N}$ width. Consider a set of independent functions $\vec{\Psi}_0^\kappa=\oplus_{j=1}^N e^{i(2\pi/N)\kappa j}\partial_s\vec{w}_0$ ($\kappa=1,2,\ldots,N$), where $\oplus_{j=1}^N$ is defined similarly to $\oplus$ and $\vec{w}_0$ is redefined by the one-stripe solution of $\frac{L}{N}$ width. Then eigenfunctions of $\mathcal{L}$ (redefined for the N-stripe solution), $\vec{\Psi}^\kappa$, are close to $\vec{\Psi}_0^\kappa$. Smooth connection of $\vec{\Psi}^{\kappa}$ at each boundary $x=\frac{L}{N}j$ is conditioned. Consideration of $Q(x)\equiv D_u\Psi_u^{\kappa}+D_v\Psi_v^{\kappa}$, which is close to $\oplus_{j=1}^{N}e^{i(2\pi/N)\kappa j}\partial_s P$, gives a rough estimation of the eigenvalues as $\lambda^{\kappa}\sim -4(\frac{N}{L})^2\partial_s P\sin^2(\frac{\pi\kappa}{N})$. This indicates that a shorter wave (i.e., closer κ to $\frac{N}{2}$) has larger instability if $\partial_s P<0$. $\lambda^{N/2}$ for even N is identical to that estimated from two stripes. Approximated values are shown in Fig. 3. The approximated λ^1 for $N=2$ is plotted in (a). Eigenvalues and corresponding eigenfunctions for $N=8, L=80.0$ are shown in (b) and (c).

To consider transient processes, an illustrative example can be seen from the stationary state of $2N$ stripes with a small perturbation. If Eq. (12) is satisfied for $\vec{w}_0$, the most unstable function is Ψ^N. By the growth of the perturbation along this function, the system reaches N-stripe pattern at last. If this new state becomes unstable, a similar process follows until the system reaches a steady state. In the (unstable) stationary state where the dynamics become close in their transient, λ is small if the distance between adjacent stripes is large. The corresponding state lasts for the duration of approximately λ^{-1} and therefore each state appears quasistationary. Because the distance becomes 2 times as large after each transient, the staying time in the quasistationary state also gets longer. We could numerically observe these processes from the eight-stripe initial condition. This demonstrates the underlying processes of the characteristic transients inherent to mass-conserved systems.

After the long transient, the system reaches the steady state at which the condition Eq. (12) is violated. Notice that Eq. (5), the condition for instability of uniform state, implies Eq. (12) is always satisfied in the early stages of transient, where $\vec{w}(x)$ ranges in the neighborhood of $\vec{w}^*$. Therefore, the characteristic wavelength of the steady state is always longer than that expected by linear stability analysis at a uniform state in a mass-conserved system. Our numerical model showed a one-stripe solution eventually between $2.0\leq L\leq 100.0$, while $\ell_m=3.2$.

One interesting question that arises is the possibility of the system in which the condition in Eq. (12) is always valid in the transient quasisteady states except in sole stripe solutions. Such systems fall into a one-stripe solution after a long transient regardless of system size. An example of such system was supplied by our group in Ref. [13], defined by $f(u,v)=-\alpha(u+v)[(\delta u+v)(u+v)-\beta]$ where $\delta=D_u/D_v$. In this specific model, if L is large enough, P is well approximated by $P=\frac{3D_v\beta}{L\gamma}\frac{1}{s}$ with $\gamma\equiv\frac{1}{2}\sqrt{\frac{D_v-D_u}{D_vD_u}}\alpha\beta$. Thus a one-stripe pattern is the only stable state in the system. Though rigorous conditions are not described here, many mass-conserved systems have such properties.

In this letter, we study RDS in which the uniform state is destabilized via a Turing-like mechanism and mass $(u+v)$ is conserved. The stability of states in such systems is derived from the condition Eq. (12). The analysis presented is useful for stationary patterns in any RDS and the conserved quantity does not have to be strictly defined by mass. Because the existence of any conserved quantity brings the corresponding 0-eigenfunction, our arguments are applicable. Thus, the dynamics studied here may be observed in a wider class of RDS with conserved quantities [12,14].

We did not mention the hierarchical structure of quasistationary states in the phase space, which is a necessary condition for the sequential transient, as discussed in Ref. [5]. It is a global property of the phase space of the systems and difficult to study. Numerical simulations suggest it is satisfied in mass-conserved systems.

Applications of this work are possible to many phenomena, particularly to biological systems. Proposed biological models often contain conserved quantities [12,15,16]. At the cellular level ($\sim 10\ \mu$m), cytosolic proteins diffuse at $\sim 10\ \mu\text{m}^2/\text{s}$ [17] leading to the rough estimation of the time scale of dynamics as $\lambda^{-1}\sim(\partial_s P/L^2)^{-1}\sim L^2/D_v\sim 10$ s. Typically, it is faster than the synthesis or degradation of molecules and the dynamics is expected to occur within the time scale in which mass-conserved modeling is valid. The formation of cell polarity based on the above discussions is a potential application [12,13,18].

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[18] M. Postma *et al.*, Mol. Biol. Cell **14**, 5019 (2003); J. Cell. Sci. **117**, 2925 (2004).
[19] We use the term "Turing-like" here because it is the limit case of usual Turing instability, but differs at $k=0$ due to the conserved property.
[20] $\vec{\phi}_4\equiv\partial_x\vec{w}_0\oplus(-\partial_x\vec{w}_0)$ is the other independent 0-eigenfunction. We do not mention it for the clarity of discussion, though one can easily discuss the stability on $\vec{\phi}_4$.