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Turing Pattern in the Oregonator Revisited

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***Abstract*—**In this paper we reconsider the analysis of the Oregonator model. We highlight an error in this analysis which leads to an incorrect depiction of the parameter region in which diffusion driven instability is possible. We believe that the cause of the oversight is the complexity of stability analyses based on eigenvalues and the dependence on parameters of matrix minors appearing in stability calculations. We regenerate the parameter space where Turing patterns can be seen, and we use the common Lyapunov function (CLF) approach, which is numerically reliable, to further confirm the dependence of the results on diffusion coefficients intensities.

***Keywords*—**Diffusion driven instability, common Lyapunov function (CLF), turing pattern, positive-definite matrix.

I. Introduction

TURING theory of pattern formation [9] has had a tremendous impact on various branches of science. According to Turing analysis a systems of reacting and diffusion chemical species, termed as *morphogens*, could lead to a spatial heterogenieties (patterns) of chemical densities from an intial uniform state. This phnomenon is known as *diffusion-driven-instability* (DDI) or Turing instability [10]. In other words Turing explanation of pattern formation is based on using a reaction diffuion (RD) system. RD models have subsequently been widely applied to various biological patterning phenomena [10], [11]. An early application of Turing's theory was to patterning of the body segment in fruity Drosophila [12], [13]. RD systems have been used to model complex pattern formation of certain animal skins [14], [15]. Reaction diffusion theory has been also utilised to examine the spatio-temporal pattern formation on the surface of tumour spheroids [16]. Pattern formation via diffusion driven instability plays an important role in chemistry [17]–[19] and physics [19]. Ecologists use RD models to understand spatial patterns in populations and communities [20]–[26], where for instance, a very fast prey (predator) would intuitively drive the density of the whole population to be spatially dependent.

Despite all the promising successes of Turing mechanism to replicate many patterns in nature, as mentioned above, existence of morphogens has not yet been proved for definite. However, there do exist very close candidates for morphogens. Calcium as morphogen leading to hair spacing in Acetabularia [27], and Fibronectin as a morphogen for cartilage formation [28]. Nevertheless, there is no definitive assertion that they are interacting as suggested by Turing. For details see [29]. In chemical systems, Turing structure has been shown by a group in Bordeaux led by De Kepper [30], [31]. The chemical reaction they used was the CIMA reaction. This paper is organised as follows. In Section II we present a classical approach for diffusion driven instability. Section III will focus on the error made during the analysis of the Oregonator model as developed by Qian et. al [1].

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II. A Classical Approach to Determining Diffusion Driven Instability

A reaction diffusion (RD) system is a system of the form

$$\frac{\partial u}{\partial t} = f(u) + D\nabla^2 u. \tag{1}$$

The function f (we assume it is regular) describes the reaction dynamics and D is a diagonal matrix of diffusion coefficients. Here $u(t,x) : [0,\infty) \times \mathbb{R}^n \rightarrow [0,\infty)$ is an n-tuple vector of densities at spatial position x and time t on a domain Ω, which typically bounded, with zero flux boundary conditions (i.e. $\nabla.u|_\Omega = 0$). Imposing such boundary conditions is due to their neutral nature as they do not pump the space with any additional material and this makes "self-organization" plausible. Taking other boundary conditions can influence the predictions where this can drive forming different patterns, see [36]. In studying pattern formation in RD systems the key first step is to determine the Turing space for a given model, i.e. the parameter set for the model on which pattern formation can be triggered [37], [38]. This can then be followed by bifurcation analysis of specific pattern formations [39]. Pattern formation is trigged by Turing instability. Turing instability, or diffusion driven instability(DDI), is a concept first proposed by Turing [9]. This concept is defined as follows.

Definition: We say that a system of the form (1) exhibits Turing instability, or DDI, if the system without diffusion, i.e.,

$$\frac{\partial u}{\partial t} = f(u). \tag{2}$$

has locally stable equilibrium state which becomes unstable in the presence of diffusion.

To analyse DDI mathematically, we use linearised stability analysis. If $\hat{u}$ is a spatially uniform equilibrium of (2), then small disturbances w away from $\hat{u}$ are governed, qualitatively, by the linear system

$$\frac{dw}{dt} = Aw.$$

Here A, the Jacobian matrix of f evaluated at $\hat{u}$, is the linearised reaction matrix. If A is stable (all its eigenvalues have negative real parts), which we assume for the remainder of this chapter, then $\hat{u}$ is an asymptotically stable equilibrium for (2). The equilibrium $\hat{u}$ is also a spatially homogeneous equilibrium of the system with diffusion. Small spatial disturbances v around $\hat{u}$ are governed by the linearised reaction diffusion equation

$$\frac{\partial v}{\partial t} = Av + D\nabla^2 v. \tag{3}$$

Now taking Fourier transform of (3) in space, following Neubert et al. [42], and using zero flux boundary conditions we obtain

$$\frac{d\check{v}}{dt} = (A - \boldsymbol{k}^2 D)\check{v} \quad (||\mathbf{k}|| = \boldsymbol{k}),$$

where

$$\check{v} = \int_{-\infty}^{\infty} e^{i\mathbf{k}.x} v(t,x)dx.$$

Here **k** is a vector of Fourier frequencies and usually referred to as the wave vector. Letting

$$J = A - \boldsymbol{k}^2 D, \tag{4}$$

Equation (3) can then be written as

$$\frac{d\check{v}}{dt} = J\check{v}.$$

Keypoint: Turing instability (DDI) requires J to be unstable for some $\boldsymbol{k}$, i.e. J has an eigenvalue with positive real part. In other words, for DDI we require

$$\rho(\boldsymbol{k}^2) := \max_{1\le i\le n} \text{real}(\lambda_i(J)) > 0 \quad \text{for some} \quad \boldsymbol{k}. \tag{5}$$

Equation (5) is often called the *dispersion relation* of the system (1). Plotting $\rho(\boldsymbol{k}^2)$ against all possible $\boldsymbol{k}^2$ is a common technique used to determine the range of unstable modes. One approach to determining this parameter set is to compute principle minors [1], [40], [41] of linearised reaction-diffusion matrices. However, this approach leads to tedious calculations in the case of high dimensional systems.

In the particular case where $n = 2$, Murray [36] derives easily verifiable necessary conditions for DDI that are also sufficient for infinite domains. In this case (1) becomes

$$\begin{aligned} \frac{\partial u}{\partial t} &= f(u,v) + d_u \nabla^2 u \\ \frac{\partial v}{\partial t} &= g(u,v) + d_v \nabla^2 v. \end{aligned}$$

The corresponding A and D in (4) are given as

$$A = \begin{pmatrix} f_u & f_v \\ g_u & g_v \end{pmatrix} \quad \text{and} \quad D = \begin{pmatrix} d_u & 0 \\ 0 & d_v \end{pmatrix}.$$

Assuming that A is stable we have

$$f_u + g_v < 0 \quad \textit{and} \quad f_u g_v - f_v g_u > 0. \tag{6}$$

In this case (4) becomes

$$J = \begin{pmatrix} f_u & f_v \\ g_u & g_v \end{pmatrix} - \boldsymbol{k}^2 \begin{pmatrix} d_u & 0 \\ 0 & d_v \end{pmatrix} = \begin{pmatrix} f_u - \boldsymbol{k}^2 d_u & f_v \\ g_u & g_v - \boldsymbol{k}^2 d_v \end{pmatrix}. \tag{7}$$

To have at least an eigenvalue with positive real part, one of the Hurwitz conditions for $A - \boldsymbol{k}^2 D$ must be violated. Conditions (6) assure that

$$\text{trace}(J) = (f_u + g_v) - \boldsymbol{k}^2(d_u + d_v) < 0.$$

So the only way to have an eigenvalue with positive real part is through the determinant. It turns out that the determinant is given by

$$\det(J) = d_u d_v \boldsymbol{k}^4 - (d_v f_u + d_u g_v)\boldsymbol{k}^2 + \det(A) =: h(\boldsymbol{k}^2). \tag{8}$$

Essentially (8) captures the signs of the dispersion relation (5) and that is why it is also called the *dispersion relation*. Since $d_u d_v \boldsymbol{k}^4$ and det(A) are positive, det(J) can be negative only if

$$d_v f_u + d_u g_v > 0. \tag{9}$$

Conditions (6) and (9) force the diffusivity coefficients to be unequal. The above condition is necessary but not sufficient for DDI. Negativity of det(J) can be assured if $h_{min}(\boldsymbol{k}^2)$ is negative. Using standard calculus techniques, we differentiate $h(\boldsymbol{k}^2)$ with respect to $\boldsymbol{k}^2$, and equating the result with zero we eventually get the stationary values

$$\boldsymbol{k}_c^2 = \frac{d_v f_u + d_u g_v}{2 d_u d_v}.$$

Substituting in (8) we get

$$h_{min} = \det(A) - \frac{(d_v f_u + d_u g_v)^2}{4 d_u d_v}.$$

Hence det(J) can be negative if, and only if,

$$(d_v f_u + d_u g_v)^2 - 4 d_u d_v \det(A) > 0.$$

Hence the necessary conditions for DDI (Turing pattern formation) are

$$\begin{aligned} f_u + g_v < 0, &\qquad f_u g_v - f_v g_u > 0, \\ d_v f_u + d_u g_v > 0, &\quad (d_v f_u + d_u g_v)^2 - 4 d_u d_v \det(A) > 0. \end{aligned} \tag{10}$$

It is worth mentioning here that the conditions (10) are also sufficient if the space is not finite which will be always the case in Section III where we do not have any restrictions on the domain. If the domain is finite then we require further investigations to the roots of (8).

III. Diffusion Driven Instability in the Oregonator

In this paper we revisit the analysis of the Oregonator performed in [1]. The Oregonator [32]–[34] is a reduced version of the oscillatory Belousov-Zhabotinsky (BZ) chemical reaction [32]. According to Feild and Noyes [33], [35], the species of the reaction behave as

$$\begin{aligned} &A + Y \longrightarrow X + P \\ &X + Y \longrightarrow P + P \\ &A + X \longrightarrow 2X + 2Z \\ &X + X \longrightarrow A + P \\ &Z \longrightarrow fY \end{aligned}$$

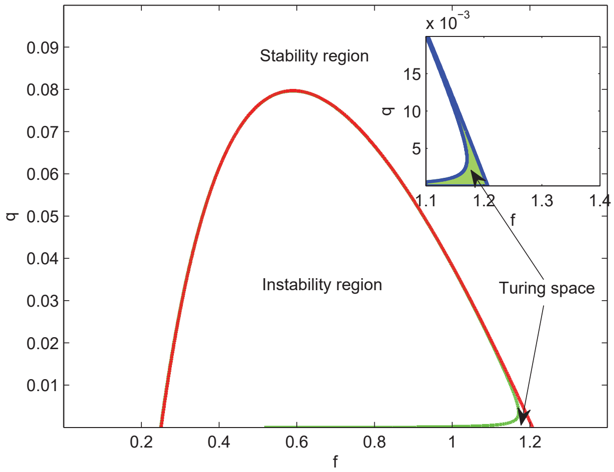

Fig. 1 The Oregonator system with parameters $\epsilon = 0.00073$, $\delta = 0.0004$. The stability region is the union of the regions outside the green or red curves. The region determined by the inequality 11 is the region inside the red curve. The region for Turing instability is the green region shown in the zoomed-in subplot

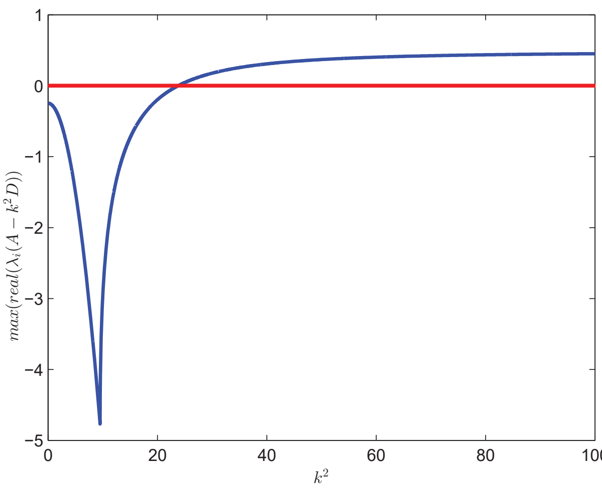

Fig. 2 The dispersion relation of the Oregonator with $f = 1.181$ and $q = 0.00226$. The remaining parameters are chosen as in Fig. 1

where $A = BrO_3^-$, $X = HBrO_2$, $Y = Br^-$, $Z = Ce(IV)$ and $P = HOBr$. The nonlinear reaction dynamics of the Oregonator are given by the system of ODEs

$$\begin{cases} \epsilon \frac{dx}{dt} &= -qy + xy + x(1-x), \\ \delta \frac{dy}{dt} &= -qy - xy + 2fz, \\ \frac{dz}{dt} &= x - z. \end{cases}$$

Here q, f, ϵ and δ are positive constants. The non-negative equilibria of the system are the origin and (x_e, y_e, z_e) where

$$\begin{cases} x_e &= 1/2\left(1 - 2f - q + \sqrt{(1-2f-q)^2 + 4q(1+2f)}\right) \\ y_e &= \frac{2fx_e}{q+x_e}, \\ z_e &= x_e. \end{cases}$$

Linearisation of the corresponding reaction-diffusion system around this uniformly steady state reduces the system to

$$\dot{z} = (A - k^2D)z,$$

where k is a wave number, $A = (a_{ij})$ is the corresponding linearised reaction matrix and $D = \text{diag}(d_i)$ is the diagonal matrix of diffusion coefficients. According to standard diffusion driven instability (DDI) calculations [9], DDI is possible when A is stable but $A - k^2D$ is unstable for some wave number k.

When A is 3×3, as is the case for the Oregonator model, stability of a matrix A can deduced from its characteristic equation

$$\lambda^3 + p_2\lambda^2 + p_1\lambda + p_0 = 0,$$

where
$p_2 = -\text{trace}(A)$, $p_1 =$ sum of the diagonal cofactors of A, and $p_0 = -\det(A)$. According to the Hurwitz criterion, A is stable if and only if

$$p_2 > 0, \quad p_0 > 0 \quad \text{and} \quad p_1p_2 - p_0 > 0.$$

In the case of the Oregonator this can be reduced to the condition

$$S := 2a_{11}a_{22} - a_{22} - a_{11} + a_{12}a_{23} - a_{11}a_{22}^2 - a_{11}^2a_{22}$$
$$+a_{11}^2 + a_{22}^2 + a_{11}a_{12}a_{21} + a_{12}a_{21}a_{22} > 0.$$

See [2], [3] for details.

To show DDI it suffices to show that A satisfies the above condition but that the matrix $A - k^2D$ violates one of the Hurwitz conditions of stability for some wave number k.

Qian and Murray use this approach to obtain sufficient conditions for DDI. In particular, they show that

$$p_0(k^2) := -\det(A - k^2D) > 0$$

is violated. Their result can be summarised as follows:

Let a_{rr} be the largest diagonal element of A and $Cof(A)_{ss}$ be the smallest diagonal cofactor of A. The sufficient condition for DDI is either

$$(i)\, a_{rr} > 0 \text{ with } \quad d_{rr} \ll 1; \quad \text{or} \quad (ii)\, Cof(A)_{ss} < 0$$

with $\;d_{ss} \gg 1$.

For the Oregonator, it turns out that the sufficient condition for DDI is given by:

$$2qy_e - (q + x_e)(1 - 2x_e) < 0 \qquad (11)$$

with relatively very large d_3. However, Qian and Murray did not verify stability of A in the same parameter region. We believe that Qian and Murray have mixed up stability of A with $\det(A) < 0$, a condition only necessary (but not sufficient) for stability of A. In fact, in the set of parameters where DDI is claimed, A itself is unstable even though $\det(A) < 0$. So DDI is not proved.

Fig. 1 shows the stability region of A (the region outside the green curve); the region determined by the inequality (11) (inside the red curve). For the specific choice of the parameters $f = 0.6$, $q = 0.03$ inside the region determined by (11) we have $\text{real}(\lambda_1(A)) = 0.002023 > 0$. So A itself is unstable and hence DDI is meaningless.

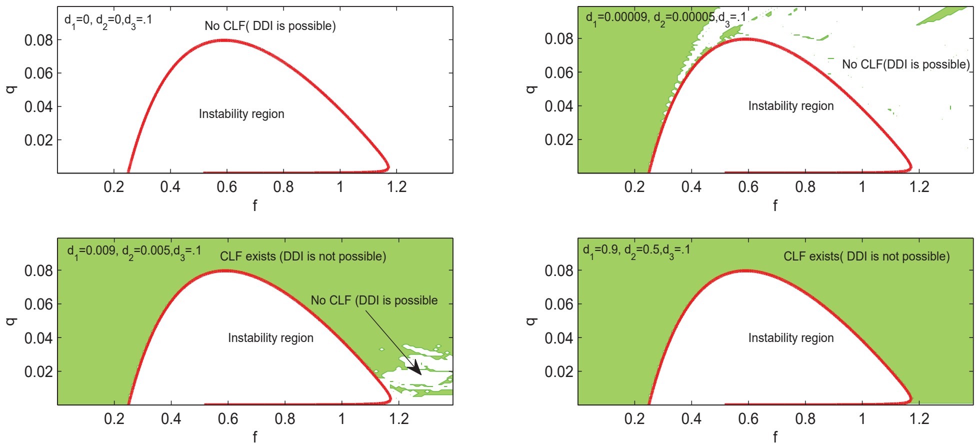

Fig. 3 The Oregonator with the same parameter chosen in above. The region where DDI is not possible (Shaded green) increases as the diffusivities $\frac{d_1}{d_3}$ and $\frac{d_2}{d_3}$ increases

Adding stability of A to the sufficient condition (11), DDI require

$$A \quad \text{is stable} \quad \text{and} \quad 2qy_e - (q + x_e)(1 - 2x_e) < 0 \qquad (12)$$

In Fig. 1, the subplot is determined by the inequalities (12). For the choice $f = 1.181$, $q = 0.00226$ in the region we have $S > 0$ and $2qy_e - (q + x_e)(1 - 2x_e) < 0$. With $d_1 = d_2 = 0$ and $d_3 = 0.9$ the corresponding dispersion relation for $A - k^2 D$ is given in Fig. 2 below which assures Turing instability approximately for $k^2 > 24$.

The Qian and Murray matrix minors based analysis of the Oregonator, needs sufficiently small diffusion coefficients. As the diffusion coefficients increase, this asymptotic analysis of stability/instability breaks down. We can use results in [2] to rule out DDI when A and $-D$ share a CLF. Fig. 3 illustrates how increasing diffusivity reduces the region in which DDI is possible.

IV. Conclusion

The Oregonator is a very well studied oscillatory chemical reaction [4]–[8]. In this paper we have revisited the analysis of the Oregonator by Qian and Murray [1]. We further confirm the dependence of the results developed in diffusion intensities using the numerical approach which based on common Lyapunove function as developed in [2]. We show that stability of the reaction matrix is not properly taken into account in generating Fig. 1 in [1]. We show, by choosing parameters in the region that A is not stable. We add the condition of stability and generate the correct picture for Turing instability, Fig. 1, and then using results from [2] we characterise the Turing region when the stability analysis of Qian and Murray does not apply, i.e., when the diffusion coefficients are very small.

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