Necessary condition of the Turing instability

L. Szili

Department of Numerical Analysis, Loránd Eötvös University, H-1117 Budapest, Bogdánfy út 10/B., Hungary

J. Tóth

Department of Computer Science, Agricultural University, H-2103 Gödöllő, Páter Károly utca 1, Hungary

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A reaction-diffusion system in any number of spatial variables consisting of an arbitrary number of chemical species cannot exhibit Turing instability if none of the reaction steps expresses cross inhibition. A corollary of this result underlines the importance of nonlinearity in the formation of stationary spatial structures, a kind of self-organization on a chemical basis.

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I. INTRODUCTION

40 years ago, in a seminal paper [1], A.M. Turing (who is well known for his achievements in computer science and in the practice of deciphering World War II codes) proposed a model for morphogenesis. He wanted to clarify how it is possible that a symmetric embryo evolves into something which is of the asymmetric form. His idea was that a reaction-diffusion system may have a stable stationary point if diffusion is not present, but by turning on diffusion the given stationary point may lose its stability and spatially inhomogeneous stable stationary patterns may emerge. The importance of this paper has mainly been recognized by theoreticians [2–11].

However, no well-defined *experiment* had been made until very recent years. All the systems exibiting spatial patterns either contained convection or surface effects, thus the origin of pattern formation has never been pure Turing instability. An important step leading to the first experimental example was the construction of the annular gel ring reactor [12], allowing the observation of chemical pinwheels (a kind of moving pattern in reaction-diffusion systems). It was putting the CIMA (chlorite iodide malonic acid) reaction into the gel ring reactor, the idea of DeKepper and his co-workers [13,14], which finally produced the long-sought-for result: the emergence of stable stationary patterns as a result of diffusive instability.

Lengyel and Epstein [15] showed that the starch indicator present in the CIMA system brings about the difference between the diffusion constants of the different chemical species which is a necessary condition of diffusive instability (cf., however, [16]).
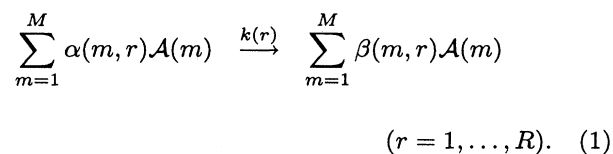
In the present paper we try to contribute to the theoretical investigation of Turing instability in the following way: we show that the presence of *cross inhibition* is a necessary condition of Turing instability. As a special case, it also turns out that the presence of higher than first-order reactions is a necessary condition, independent of the number of chemical species. This statement is an extension of earlier results on three-species systems which have been obtained using elementary methods by the authors [17].

First, we summarize the theoretical framework for the investigation of diffusive instabilities in reaction-diffusion systems. Second, we formulate the mathematical statement implying our main result. Finally, we show that the usually investigated models giving rise to Turing instability do contain cross inhibition in accordance with our results.

II. TURING INSTABILITY IN REACTION-DIFFUSION SYSTEMS

A. Reaction-diffusion systems

Let us consider a vessel, i.e., a finite simply connected domain Ω in $\mathbb{R}^N$ (N is an arbitrary positive integer, the number of spatial dimensions) in which diffusion and chemical reaction steps take place. Let us suppose that the chemical species occurring anytime during the reaction are $\mathcal{A}(1), \ldots, \mathcal{A}(M)$ ($M \in \mathbb{N}$). Among the chemical species the following $R \,(\in \mathbb{N})$ reaction steps take place:

$$\sum_{m=1}^{M} \alpha(m,r)\mathcal{A}(m) \xrightarrow{k(r)} \sum_{m=1}^{M} \beta(m,r)\mathcal{A}(m)$$

$$(r = 1, \ldots, R). \quad (1)$$

The non-negative integers $\alpha(m,r)$ and $\beta(m,r)$ are called *stoichiometric coefficients.*

The usual mathematical model for this process, taking into account diffusion of the species, is the system of partial differential equations

$$\frac{\partial c_m(t,\mathbf{x})}{\partial t} = f_m(\mathbf{c}(t,\mathbf{x})) + D_m \triangle c_m(t,\mathbf{x})$$

$$(m = 1, \ldots, M) \quad (2)$$

where $c_m(t,\mathbf{x})$ is the concentration of species $\mathcal{A}(m)$ at time t at the location $\mathbf{x} \in \Omega$,

$$\mathbf{c}(t,\mathbf{x}) := (c_1(t,\mathbf{x}), \ldots, c_M(t,\mathbf{x})),$$

$D_m \in \mathbb{R}^+ := \{x \in \mathbb{R}', x > 0\}$ is the diffusion constant of

species $\mathcal{A}(m)$,

$$f_m(\mathbf{c}) := \sum_{r=1}^{R} [\beta(m,r) - \alpha(m,r)] w_r(\mathbf{c}),$$

and $w_r(\mathbf{c})$ is the rate of the rth reaction step at the concentration $\mathbf{c}$ supposed to be continuously differentiable (see Ref. [18]).

From now on we require that $w_r(\mathbf{c}) > 0$ whenever supp $\mathbf{c} \supset$ supp $\alpha(\cdot, r)$ and that $w_r(\mathbf{c}) = 0$ whenever there exists m such that $c_m = 0$ and $\alpha(m,r) > 0$. This is the formal expression of the natural requirement that reaction step r takes place (proceeds with nonzero rate) if and only if all its reactant (:=left-hand-side) species are present (in nonzero concentration).

The most often used form of w_r is of the *mass-action type* when there exist positive numbers k_r $(r = 1, \dots, R)$ such that $w_r(\mathbf{c}) := k_r \prod_{p=1}^{M} c_p^{\alpha(p,r)}$ $\left(=: k_r \mathbf{c}^{\alpha(\cdot, r)} \right)$. Mass-action-type reaction rates obviously fulfill the two requirements stated above.

In order to uniquely define the system, initial and boundary conditions are to be specified. We take the initial conditions

$$c_m(0, \mathbf{x}) = c_m^0(\mathbf{x}) \qquad (\mathbf{x} \in \Omega; m = 1, \dots, M) \qquad (3)$$

and we can either take *fixed boundary conditions*

$$c_m(t, \mathbf{x}) = c_m^* \qquad (\mathbf{x} \in \partial\Omega; \ m = 1, \dots, M), \qquad (4)$$

where c_m^* is the m-th coordinate of the homogeneous steady state (see the formal definition below), or the *zero-flux boundary conditions*

$$\langle \nabla c_m(t, \mathbf{x}), \nu(\mathbf{x}) \rangle = 0 \quad (\mathbf{x} \in \partial\Omega; \ m = 1, \dots, M), \qquad (5)$$

where $\nu(\mathbf{x})$ denotes the outer normal to $\partial\Omega$ at the point $\mathbf{x} \in \partial\Omega$.

Astonishing as it may seem from the mathematical point of view, numerical and experimental investigations show no essential differences betwen the two cases, if the size of the vessel is much larger than the characteristic wavelength. Usually the emerging structures differ only in phase.

B. Turing instability

The first constituent of Turing instability is that there exists a non-negative steady-state solution $\mathbf{c}^*$ to the *kinetic differential equation*

$$\dot{\mathbf{c}}(t) = \mathbf{f}(\mathbf{c}(t)), \qquad (6)$$

where $\mathbf{f} := (f_1, \dots, f_M)$ is defined by the first term on the right-hand side of (2). In other words, $\mathbf{c}^*$ satisfies $\mathbf{f}(\mathbf{c}^*) = \mathbf{0}$. It is assumed here that the real parts of all the eigenvalues of the Jacobian $\mathbf{f}'(\mathbf{c}^*)$ are negative.

Let us introduce

$$\sigma(A) := \{ \lambda \in \mathbf{C} ; \ \lambda \text{ is an eigenvalue of } A \}$$

for the *spectrum* of an arbitrary matrix $A \in \mathbb{R}^{M \times M}$, and let

$$s(A) := \max\{ \mathrm{Re} \, \lambda ; \ \lambda \in \sigma(A) \}$$

be the *spectral abscissa* of A. Then the assumption is just

$$s(\mathbf{f}'(\mathbf{c}^*)) < 0. \qquad (7)$$

This is a sufficient condition (but it is only necessary in the case of a linear $\mathbf{f}$) of the asymptotic stability of the steady state $\mathbf{c}^*$ of the kinetic differential equation describing the spatially homogeneous case. Inequality (7) obviously implies that the solution to the full nonlinear reaction-diffusion system (2), (3), and (4) or (5) returns to the spatially homogeneous state $\mathbf{c}^*$ after a small spatially homogeneous perturbation.

Let Ω be a sufficiently regular bounded domain in $\mathbb{R}^N$. It is known that all eigenvalues $\kappa_0, \kappa_1, \dots$ of the Laplace operator on Ω under both the given boundary conditions are negative. Martin ([19], proposition 2) has shown that if for all $k = 0, 1, \dots$

$$s(\mathbf{f}'(\mathbf{c}^*) + \kappa_k D)) < 0 \qquad (8)$$

with $D := \mathrm{diag}(D_1, \dots, D_M)$, then $\mathbf{c}^*$ is a globally uniformly asymptotically stable solution of the nonlinear reaction-diffusion equation (2) in the maximum norm.

If condition (7) is fulfilled and there exists κ_k for which (8) does not hold, then we say that the system (2) shows *Turing instability*. This may imply that stable inhomogeneous stationary patterns emerge in the original nonlinear system (2). This phenomenon has been observed numerically, but a global analytical investigation of the nonlinear system seems to be quite difficult even in simple special cases.

C. The absence of negative cross effects

Before investigating some simpler cases in detail, another important notion has to be introduced. The kinetic differential equation (6), of the mass-action type, is a polynomial differential equation, but not all polynomial differential equations may be considered to be models of chemical reactions [20].

Let us consider Turing's example [1]:

$$\dot{x} = 5x - 6y + 1, \quad \dot{y} = 6x - 7y + 1. \qquad (9)$$

The term $-6y$ on the right-hand side of the first equation expresses the fact that x decreases in a process in which it does not take part, or expresses a *negative cross effect*. Kinetic differential equations are characterized by the absence of such terms. This characterisation has proved quite useful to study kinetic gradient systems [21], to design oscillatory reactions [22], or to investigate chaos in chemical reactions [23].

Suppose we have only first-order reactions, i.e.,

$$\sum_{m=1}^{M} \alpha(m,r) \leq 1 \qquad \text{for all } r = 1, \dots, R.$$

Then, the absence of negative cross effects implies that the coefficient matrix A of the right-hand side of the ki-

netic differential equation is an *essentially non-negative* matrix, i.e.,

$$a_{mp} \geq 0, \qquad m, p = 1, \ldots, M; \quad m \neq p. \tag{10}$$

Obviously, in the case of first-order reactions with mass-action-type reaction rates we have $A = \mathbf{f}'(\mathbf{c}^*)$ for any $\mathbf{c}^* \in \mathbb{R}^M$.

D. Special cases

Now let us turn to the recapitulation of special cases. If $M = 1$, then $s(\mathbf{f}'(\mathbf{c}^*)) = \mathbf{f}'(\mathbf{c}^*)$, therefore (7) implies (8) for any kind of reaction.

If $M = 2$ and the reactions are of the first order with mass-action-type reaction rates, then (7) is equivalent to stating

$$a_{11} + a_{22} < 0 \tag{11}$$

and

$$\det(A) := a_{11}a_{22} - a_{12}a_{21} > 0. \tag{12}$$

Inequality (12) can only hold if $a_{11}a_{22} > 0$ because of the essential non-negativity of A. Taking into consideration (11) one obtains $a_{11} < 0$ and $a_{22} < 0$. Therefore, for all $c_1, c_2 \in \mathbb{R}^+$

$$a_{11} + a_{22} - (c_1 + c_2) < 0 \tag{13}$$

and

$$\det(A) - (c_1 a_{22} + c_2 a_{11}) + c_1 c_2 > 0. \tag{14}$$

Inequalities (13) and (14) together imply (8) if one takes $c_1 := -\kappa_k D_1, c_2 := -\kappa_k D_2$. The same argument can be applied to the more general case when one assumes the absence of cross inhibition instead of assuming that the reaction steps are of the first order as in this case $A := \mathbf{f}'(\mathbf{c}^*)$ is essentially non-negative.

It can be shown using an elementary argument that first-order reactions with mass-action-type reaction rates are not enough to evoke Turing instability even in the case $M = 3$ [17]. Jacimirsky [24] and Li and Wu [25] have found that three species with higher-order formal reactions may produce Turing instability.

III. MAIN RESULT

The matrix $A \in \mathbb{R}^{M \times M}$ is said to be *non-negative* if every element of A is non-negative. An $M \times M$ real matrix A with non-negative elements off the main diagonal is called *essentially non-negative*.

The following definitions and statements are needed for the proof of the main result (see [26,27]).

The *spectral radius* of a matrix $A \in \mathbb{R}^{M \times M}$ is defined as

$$\varrho(A) := \max\{ |\lambda| \; : \; \lambda \in f_{\text{spec}}(A)\}.$$

Let $A \in \mathbb{R}^{M \times M}$ be a non-negative matrix. Then the following statements hold. (i) $\varrho(A)$ is an eigenvalue of A and the spectral radius of A is equal to the spectral abscissa of A, i.e., $\varrho(A) = r(A)$; (ii) if, in addition, B

also is a non-negative matrix, then

$$\varrho(A + B) \geq \varrho(A).$$

Our main tool will be the statement below.

Theorem. Let us suppose that for the essentially non-negative matrix $A \in \mathbb{R}^{M \times M}$ $s(A) < 0$ holds, and that C is a diagonal matrix with non-negative elements on the main diagonal. Then $s(A - C) < 0$ also holds.

Proof. We prove first the following statement: if $A \in \mathbb{R}^{M \times M}$ is an essentially non-negative matrix and $C = \text{diag}(c_1, \ldots, c_M) \in \mathbb{R}^{M \times M}$ is a non-negative diagonal matrix, then $s(A + C) \geq s(A)$.

Let us introduce

$$K := \max\{c_m - a_{mm} \; ; \; m = 1, \ldots, M\}.$$

Then $A - C + KI$ is non-negative and the statement is implied by the following series of inequalities and equalities:

$$\begin{aligned}
s(A) + K = s(A + KI) &= \varrho(A + KI) \\
&\geq \varrho(A - C + KI) = s(A - C + KI) \\
&= s(A - C) + K.
\end{aligned}$$

For the proof of our main result assume that there exists an eigenvalue κ of the Laplace operator on Ω under the given boundary conditions such that $s(A + \kappa D) \geq 0$. Since $-\kappa D$ is a non-negative matrix, we have that

$$s(A) = s((A + \kappa D) - \kappa D) \geq s(A + \kappa D) \geq 0,$$

contradicting the condition $s(A) < 0$. This completes the proof of our main result.

The reaction (1) is said to contain *cross inhibition* at the concentration $\mathbf{c} \in \mathbb{R}^M$ if there exist $m, p \in \{1, \ldots, M\}$; $m \neq p$ for which $\partial_m f_p(\mathbf{c}) < 0$ holds.

A reaction without containing cross inhibition has an essentially non-negative Jacobian $\mathbf{f}'(\mathbf{c})$ at all concentrations $\mathbf{c}$. Thus, the theorem above immediately implies the statement below.

Corollary 1. Suppose that reaction (1) does not contain cross inhibition. Then it cannot show Turing instability either.

Obviously, reaction (1) endowed with mass-action-type reaction rates does not contain cross inhibition if for all $r \in \{1, \ldots, R\}$ either $\beta(\cdot, r) \geq \alpha(\cdot, r)$ is true or, if there exist $p \in \{1, \ldots, M\}$ for which $\beta(p, r) < \alpha(p, r)$, then for all $m \neq p$, $m \in \{1, \ldots, M\}$, $\alpha(m, r) = 0$.

The chemical meaning of this property is that a reaction step containing cross inhibition is a step in which the rate of decrease of a chemical species is negative in the presence of another species.

Since first-order reactions induce a linear kinetic differential equation with an essentially non-negative coefficient matrix, we obtain the following

Corollary 2. First-order reactions with mass-action-type reaction rates cannot show Turing instability.

IV. EXAMPLES

A reaction only consisting of steps of the type

$$\alpha(m, r)\mathcal{A}(m) \longrightarrow \beta(m, r)\mathcal{A}(m)$$
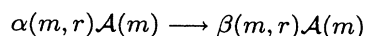
$(r = 1, \ldots, R; \; m = 1, \ldots, M)$

is said to be a *generalized compartmental system*. Such a reaction does not contain cross inhibition.

The model by Gierer and Meinhardt [3] given by

$$f_1(\bar{c}_1, \bar{c}_2) := k_1 - k_2\bar{c}_1 + k_3\bar{c}_1^2/\bar{c}_2,$$
$$f_2(\bar{c}_1, \bar{c}_2) := k_4\bar{c}_1^2 - k_5\bar{c}_2$$

does contain cross inhibition as $\partial_2 f_1(\bar{c}_1, \bar{c}_2) = -k_3\bar{c}_1^2/\bar{c}_2^2$.

Turing's example (9) does contain cross inhibition, as it does contain a negative cross effect: $\partial_2 f_1(x, y) = -6 < 0$.

It can easily be shown that all the other (cited and not cited) models showing Turing instability do contain cross inhibition in accordance with our result [28–32].

ACKNOWLEDGMENTS

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