

## **Review Report on the doctoral dissertation**

### **Patterns in nonlocal and degenerate models from mathematical biology**

**submitted by Szymon Cygan**

This dissertation is concerned with pattern formation in mathematical models of biology and has three main subjects: (1) nonlocal models, (2) smooth stationary solutions of reaction-diffusion-ODE systems and (3) stationary solutions with jump discontinuity of reaction-diffusion-ODE systems.

#### **1. A class of nonlocal models for biological pattern formation (Chapter 2)**

In the seminal paper “The chemical basis of morphogenesis” Turing claimed that reaction between two species of chemicals with different diffusion rates may cause the instability of spatially uniform states, leading to spontaneous formation of nontrivial spatial structure. Gierer and Meinhardt developed this idea and proposed a reaction-diffusion system composed of a short-range activator and a long-range inhibitor. Here, “short range” means a small diffusion coefficient and “long range” corresponds to a large diffusion coefficient. Lately Kondo proposed a nonlocal model which incorporates short-range activation and long-range inhibition in a single equation. Kondo’s model was derived with very heuristic reasoning and hence systematic and theoretical studies are needed to justify the model.

Cygan has given a mathematical foundation for rigorous treatment of a class of nonlocal equations including Kondo’s model by proving the existence of stationary solution in one dimensional domains. Numerical simulations in one-dimensional domains and two-dimensional domains are provided for various kernel functions, which suggest future directions of research.

#### **2. Reaction-diffusion-ODE systems (Chapters 3–6)**

“Pattern” means nontrivial spatial structure with a certain degree of order or regularity. Consider, for instance, several species of substances distributed in a cell assemblage. If no species diffuses, lack of cell-to-cell communication prevents formation of pattern. At least one species has to diffuse for pattern formation. It is expected that the more species diffuse, the more strongly pattern is ordered. The second theme of this dissertation is pattern formation in systems where there is only one diffusive species, that is, one reaction-diffusion equation coupled with  $n$  ordinary differential equations.

## 2.1. Instability of regular stationary solutions of reaction-diffusion-ODE systems (Chapter 4)

In this chapter, a general reaction-diffusion-ODE system  $U_t = f(U, V)$ ,  $V_t = \Delta V + g(U, V)$  is considered, where  $U(x, t)$  is an  $\mathbb{R}^n$ -valued function and  $V(x, t)$  is an  $\mathbb{R}$ -valued function,  $x \in \Omega$ , a bounded domain in  $\mathbb{R}^N$ , and  $\Delta$  is the Laplace operator subject to the homogeneous Neumann boundary condition. If the system has a constant stationary solution  $(\bar{U}, \bar{V})$ , under certain assumptions on the linearization around  $(\bar{U}, \bar{V})$ , a family of nonconstant *smooth* stationary solutions to a perturbed problem bifurcates from  $(\bar{U}, \bar{V})$ . Moreover, it is proved that for a smooth non-constant stationary solution  $(U(x), V(x))$ , if the matrix  $f_u(U(x_0), V(x_0))$  has an eigenvalue with positive real part for some  $x_0 \in \Omega$ , then  $(U(x), V(x))$  is unstable in the topology of  $C(\bar{\Omega})^{n+1}$ . In addition, even if all eigenvalues of the  $n \times n$  matrix  $f_u(U(x), V(x))$  have negative real part for any  $x \in \bar{\Omega}$ , the convexity of the domain  $\Omega$  implies the instability of  $(U(x), V(x))$ . The last result is a generalization of classical Casten-Holland's theorem.

These results are generalization of the case  $n = 1$  and  $N = 1$ , i.e., one reaction-diffusion equation coupled with one ordinary differential equation in one-dimensional domains.

## 2.2. Existence of stable stationary solutions with jump discontinuity (Chapter 5)

The existence of stable non-constant stationary solutions is addressed in this chapter. Consider the system  $U_t = f(U, V)$ ,  $V_t = \gamma \Delta V + g(U, V)$  with diffusion coefficient  $\gamma > 0$ . Assume that the system has a constant stationary solution  $(\bar{U}, \bar{V})$  and the linearized operator around  $(\bar{U}, \bar{V})$  satisfies some conditions on the spectrum. Moreover, it is assumed that the algebraic equation  $f(U, V) = 0$  has two different branches of solutions:  $f(k_j(V), V) = 0$ ,  $j = 1, 2$ , for  $V \in \mathcal{V}$  where  $\mathcal{V}$  is a neighborhood of  $\bar{V}$ ,  $k_j \in C^2(\mathcal{V}, \mathbb{R}^n)$ ,  $\bar{U} = k_1(\bar{V})$  and  $k_1(\bar{V}) \neq k_2(\bar{V})$ . Then there exists an  $\epsilon$ -dependent family of non-constant stationary solutions  $(U_\epsilon(x), V_\epsilon(x))$  and decomposition of  $\Omega$  into two disjoint open subsets  $\Omega_1$  and  $\Omega_2$  (i.e.,  $\Omega \subset \overline{\Omega_1 \cup \Omega_2}$ ) with  $|\Omega_2| = O(\epsilon)$  such that  $U_\epsilon(x)$  is  $\epsilon$ -close to  $U_1$  uniformly on  $\Omega_1$  and to  $k_2(\bar{V})$  uniformly on  $\Omega_2$ , whereas  $V_\epsilon(x)$  is in  $C^1(\bar{\Omega})$  and  $\epsilon$ -close to  $\bar{V}$  uniformly on  $\bar{\Omega}$ . It is to be emphasized that the choice of open subsets  $\Omega_1$  and  $\Omega_2$  is arbitrary as long as the smallness condition on  $|\Omega_2|$  is satisfied, besides the discontinuity of  $U_\epsilon(x)$ . Moreover, under additional conditions on the spectrum of the linearized operators around  $(\bar{U}, \bar{V})$  and  $(k_2(\bar{V}), \bar{V})$ , it is proved that  $(U_\epsilon(x), V_\epsilon(x))$  is exponentially asymptotically stable in  $L^\infty(\Omega)^{n+1}$  for sufficiently large diffusion coefficient  $\gamma$ .

Due to the jump-discontinuity in  $U(x)$ , noticeable patterns appear in the distribution of non-diffusive species. Moreover, It is important to point out that we can design the pattern by choosing  $\Omega_1$  and  $\Omega_2$  appropriately. In Chapter 6, this is demonstrated numerically for specific two-species models. It provides an impressive difference from the system without non-diffusive species, where the geometry of domain  $\Omega$  plays a crucial role.

In this dissertation, Cygan has obtained pioneering and important results on the nonlocal models and on general reaction-diffusion-ODE systems in higher dimensional domains. Their contribution to the field of mathematical analysis of pattern formation in biology is of great significance. The approaches developed and the results obtained here will certainly open the door to a new phase of researches on pattern formation in reaction-diffusion-ODE systems.

Consequently, the reviewer regards, without hesitation, this dissertation as an excellent piece of work.

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A handwritten signature in black ink, reading "Izumi Takagi". The signature is written in a cursive style with a large initial 'I' and 'T'.

Izumi Takagi