Institute of Physics Publishing
doi:10.1088/1742-6596/55/1/012

Journal of Physics: Conference Series **55** (2006) 130–134
International Workshop on Multi-Rate Processes and Hysteresis

Hysteresis in biological models

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Abstract. The paper gives an overview of results for partial differential equations with hysteresis whose motivation comes from biology.

1. Introduction

In the biological literature, there are examples of processes whose state variables change due to a change of parameters in such a way that when the parameters go back to the old values the system does not follow its steps in reverse and thus a hysteresis loop is formed. Also many biological problems involve a fold catastrophe regime which can be replaced by a model involving hysteresis [8].

Although during the last decades there has been a steady growth in the mathematical study of various hysteresis operators and applications, the mathematical treatment of biological problems with hysteresis has been considered so far in few papers.

It is the purpose of the present paper to give an overview of such biological problems studied from a mathematical point of view.

2. Model for bacterial growth

A model for bacterial growth patterns was the first biological model involving hysteresis which was studied mathematically [5], [6], [7].

Similar to the classical experiment for Liesegang phenomena in chemical precipitation, concentrical growth rings were observed in response to a diffusing front of histidine auxotrophic salmonella typhimurium spreading from the center of a Petri dish to its boundary. Here the bacteria are immobile, they are fixed on an agar gel containing all chemicals necessary for growth except the missing amino acid. Therefore the spatial interaction is caused only by diffusion of the nutrients and the buffer neutralized by acids produced as byproducts of the cell growth.

Let us note that in an attempt to better understand the mechanism for the formation of concentric rings of growth, additional insight into the process was sought using the technique of mathematical modelling, see e.g. [13]. To explain the periodic structure a mathematical model with hysteresis was suggested in [5].

With the assumption that there exist thresholds for growth expressed in terms of the concentration of chemicals, i.e., there is no growth until a certain threshold is reached and the growth continues even as the system is falling below this threshold until a second threshold is reached where the growth stops, the model was described mathematically in [6] by a system of partial differential equations of the following type:

$$\frac{\partial B}{\partial t} = \alpha V B, \qquad \text{in } \Omega \times (0,T) \tag{1}$$

$$\frac{\partial H}{\partial t} = D_H \triangle H - \beta V B, \qquad \text{in } \Omega \times (0,T) \tag{2}$$

$$\frac{\partial G}{\partial t} = D_G \triangle G - \gamma V B, \qquad \text{in } \Omega \times (0,T), \tag{3}$$

where H describes the histidine concentration, G the concentration of the growth mediums buffer and B the size of the bacterial population. V is a function describing the metabolic activity of bacteria. It is assumed that the cell growth continues until the combination of H and G reaches a threshold value at which cell growth stops, growth does not begin again until a higher threshold is reached. This is modelled with a hysteresis operator of relay type.

Here $\alpha, \beta, \gamma, D_H, D_G$ are given positive constants, large compared to the positive diffusivity constants D_H, D_G, and Ω is a bounded region in R^n with smooth boundary $\partial\Omega$.

The system (1)-(3) was coupled with the following boundary and initial conditions:

$$\frac{\partial H}{\partial \nu} = \frac{\partial G}{\partial \nu} = 0 \text{ on } \partial\Omega \times (0,T), \tag{4}$$

$$B(x,0) = B_0(x), H(x,0) = H_0(x), G(x,0) = G_0(x) \text{ on } \Omega, \tag{5}$$

where ν is the outward unit normal vector to the boundary.

In [6], [5] numerical results for this model were presented giving a very good correspondence with biological experiments. The mathematical problem, however, was never solved. An attempt has been made by A. Visintin, [11], where a simplified model

$$\frac{\partial B}{\partial t} = \alpha V \tag{6}$$

$$\frac{\partial H}{\partial t} = D_H \triangle H - \beta V \tag{7}$$

$$\frac{\partial G}{\partial t} = D_G \triangle G - \gamma V \tag{8}$$

was shown to have a solution by approximation, a priori estimates and a limit procedure. An existence result for the system (1)-(3) was not proved until recently, [1]. Note that uniqueness, because of the presence of the hysteresis operator of the type of completed relay in the source term, is not expected, see [12].

The hysteresis relation can be described mathematically as follows: Let ψ_{on}, ψ_{off} be functions on R^2 satisfying $\psi_{off} \geq \psi_{on}$ on R^2, ψ_{off} will denote the threshold at which cell growth stops and ψ_{on} denotes that at which cells begin to grow again. We will use the following notation

$$\Gamma_{on} = \{(H,G); \psi_{on}(H,G) = 0\}, \tag{9}$$

$$\Gamma_{off} = \{(H,G); \psi_{off}(H,G) = 0\}, \tag{10}$$

$$M_{on} = \{(H,G); \psi_{on}(H,G) > 0\}, \tag{11}$$

$$M_{off} = \{(H,G); \psi_{off}(H,G) < 0\}, \tag{12}$$

$$M_{on-off} = \{(H,G); 0 \leq \psi_{off}(H,G), \psi_{on}(H,G) \leq 0\}, \tag{13}$$

$$M^*_{on} = M_{on} \cup \Gamma_{on}, \tag{14}$$

$$M^*_{off} = M_{off} \cup (\Gamma_{off}/\Gamma_{on}), \tag{15}$$

$$M = \{(H,G); 0 < \psi_{off}(H,G), \psi_{on}(H,.G) < 0\}. \tag{16}$$

Definition 2.1. *For any* $(H,G) \in [C^0([0,T])]^2$ *and any initial state* $\xi \in \{0,1\}$ *we define the (single valued) function* $S = S(H,G,\xi) : [0,T] \to \{0,1\}$ *as follows:*

$$S(0) = \begin{cases} 0 & \textit{if } (G(0),H(0)) \in M^*_{off} \\ \xi & \textit{if } (H(0),G(0)) \in M \\ 1 & \textit{if } (H(0),G(0)) \in M^*_{on} \end{cases}$$

for any $t \in (0,T]$*, and setting* $X_t = \{\tau \in (0,T],\ (H(t),G(t)) \in \Gamma_{on} \textit{ or } \Gamma_{off}\}$,

$$S(t) = \begin{cases} S(0) & \textit{if } X_t = \emptyset \\ 0 & \textit{if } X_t \neq \emptyset \textit{ and } (H(maxX_t),G(maxX_t)) \in \Gamma_{off} \\ 1 & \textit{if } X_t \neq \emptyset \textit{ and } (H(maxX_t),G(maxX_t)) \in \Gamma_{on}, \end{cases}$$

see Figure 1.

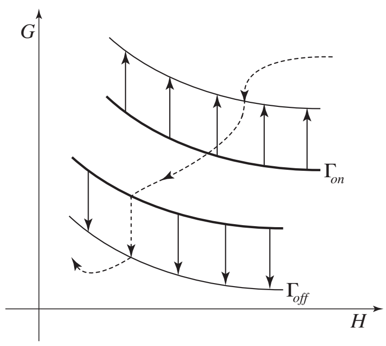

Figure 1. The hysteresis operator

Notice the similarity with the definition of a classical relay operator, see e.g. [12] for more details.

It can be shown that the operator S is not closed with respect to the strong topology of $[C^0([0,T])]^2$ for the input (H,G) and the weak star topology of $BV(0,T)$ for the output S.

Then the operator $\tilde{S} : [C^0([0,T])]^2 \times [0,1] \to \mathcal{P}(BV(0,T))$ is defined as follows:

$$\tilde{S}(0) = \begin{cases} \{0\} & \text{if } (H(0),G(0)) \in M_{off} \\ [0,\xi] & \text{if } (H(0),G(0)) \in \Gamma_{off} \\ \{\xi\} & \text{if } (H(0),G(0)) \in M \\ [\xi,1] & \text{if } (H(0),G(0)) \in \Gamma_{on} \\ \{1\} & \text{if } (H(0),G(0)) \in M_{on} \end{cases}$$

$$\tilde{S}(t) = \begin{cases} \{0\} & \text{if } (H(t),G(t)) \in M_{off} \\ [0,1] & \text{if } (H(t),G(t)) \in M_{on-off} \\ \{1\} & \text{if } (H(t),G(t)) \in M_{on} \end{cases}$$

$$\begin{cases} \text{if } (H(t),G(t)) \neq \Gamma_{on},\Gamma_{off}, & \text{then } \tilde{S} \text{ is constant in a neighbourhood of } t \\ \text{if } (H(t),G(t)) \in \Gamma_{off}, & \text{then } \tilde{S} \text{ is nonincreasing in a neighbourhood of } t \\ \text{if } (H(t),G(t)) \in \Gamma_{on}, & \text{then } \tilde{S} \text{ is nondecreasing in a neighbourhood of } t. \end{cases} \tag{17}$$

The hysteresis relation is assumed to hold pointwise in space $V(x,t) = \tilde{S}(H(x,\cdot),G(x,\cdot))(t)$.

For the existence proof, the relay type hysteresis operator is in [1] approximated by a sequence of operators of play type which can be represented as differential inclusions:

$$\frac{\partial V}{\partial t} + \partial I_\epsilon(G, H; V) \ni 0, \tag{18}$$

where $I_\epsilon(G, H; \cdot)$ is the indicator function of the closed interval $[f_{*\epsilon}, f^*_\epsilon]$, f_* and f^* are functions on R^2 such that $f_* = 1$ on M^*_{on} and $f_* = 0$ otherwise, $f^* = 0$ on M^*_{off} and $f^* = 1$ otherwise, and $\{f_{*\epsilon}\}$ and $\{f^*_\epsilon\}$ are sequences of $C^2(R^2)$ functions approximating it, i.e. $f_{*\epsilon}(x) \to f_*(x)$ and $f^*_\epsilon(x) \to f^*(x)$ as $\epsilon \to 0$ for each $x \in R^2$. It is well known that the differential inclusion (18) is equivalent to the classical play operator.

Theorem 2.1. *If the Assumptions* $(A1)$ - $(A3)$

(A1) $B_0, H_0, G_0 \in L^\infty(\Omega)$

(A2) $B_0 \geq 0, H_0 \geq 0, G_0 \geq 0$.

(A3) $f_*(H_0, G_0) \leq V_0 \leq f^*(H_0, G_0)$.

are satisfied, there exists at least one solution of the system $(1) - (3)$ *coupled with initial conditions* (5) *and boundary conditions* (4) *and* V *a solution of (18).*

The theorem is proved using the standard technique of Yosida approximation, deriving uniform bounds and limit procedure.

3. Prey-predator systems with hysteresis

In [2] a system of nonlinear PDEs with diffusive as well as hysteresis effects is suggested to model the evolution of populations. The model originates from a prey-predator model of the following type:

$$\begin{aligned} \sigma &= \lambda(u) \quad \text{in } \Omega \times (0,T) && (19)\\ \frac{\partial u}{\partial t} - \triangle u &= h(\sigma, u, v) \quad \text{in } \Omega \times (0,T) && (20)\\ \frac{\partial v}{\partial t} - \triangle v &= g(\sigma, u, v) \quad \text{in } \Omega \times (0,T). && (21)\\ & && (22) \end{aligned}$$

Here σ denotes the density of the quality of food for the prey, u and v are densities of the prey and predator, respectively and Ω is a bounded region in R^n with smooth boundary $\partial\Omega$.

The speed of change of the density of food when the density of the prey decreases is different from the speed when the density of the prey increases, i.e. the state of the system depends on the previous evolution of data. Also when a small diffusive effect for the food of the prey is considered a more complicated model is obtained:

$$\begin{aligned} \frac{\partial \sigma}{\partial t} - \frac{\partial \lambda(u)}{\partial t} - k\triangle\sigma + \partial I_{u,v}(\sigma) &\ni F(\sigma, u, v) \quad \text{in } \Omega \times (0,T) && (23)\\ \frac{\partial u}{\partial t} - \triangle u &= h(\sigma, u, v) \quad \text{in } \Omega \times (0,T) && (24)\\ \frac{\partial v}{\partial t} - \triangle v &= g(\sigma, u, v) \quad \text{in } \Omega \times (0,T), && (25) \end{aligned}$$

where $I_{u,v}(\cdot)$ denotes the indicator function of a closed interval $[f_*(u,v), f^*(u,v)]$, $f_*(u,v)$ and $f^*(u,v)$ are C^2 functions, $0 \leq f_*(u,v) \leq f^*(u,v) \leq 1$, $\partial I_{u,v}(\cdot)$ is the subdifferential of $I_{u,v}(\cdot)$

Let us note that if σ is the solution of the differential inclusion

$$\frac{\partial \sigma}{\partial t} - \frac{\partial u}{\partial t} + \partial I_u(\sigma) \ni 0 \text{ in } \Omega \times (0,T), \tag{26}$$

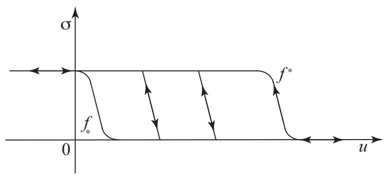

Figure 2. Generalized stop operator

then σ is the output of the hysteresis operator of stop type, see Figure 2.

This fact was pointed in [12] and used in many papers for the analysis of nonlinear phenomena, e.g. in real-time control problems, or solid-liquid phase transition where hysteresis effects are taken into account. The paper [2] is devoted to a detailed analysis of the system (23) -(25). Results for positivity, boundedness, existence and uniqueness of solutions of the prey-predator model are obtained. Under appropriate assumptions, using the method of Yosida approximation combined with the derivation of appropriate uniform bounds, the authors prove that there exists at least one solution of the system. Uniqueness is obtained for $n \leq 3$.

In [10] a more complicated system for population dynamics is analyzed, taking also convective terms into account:

$$\frac{\partial \sigma}{\partial t} - \nabla \cdot (\nabla \sigma + \lambda(\sigma)) + \partial I_U(\sigma) \ni g(\sigma, U) \quad \text{in } \Omega \times (0,T) \tag{27}$$

$$\frac{\partial u_i}{\partial t} - \nabla \cdot (\nabla u_i + \mu_i(u_i)) = h_i(\sigma, U) \quad \text{in } \Omega \times (0,T), \tag{28}$$

where $U = (u_1, \ldots, u_m)$.

Results for non-negativity, boundedness and existence of at least one solution of the population model with hysteresis effect are obtained. The main tools are the method of Yosida approximation, the energy method for parabolic systems and fixed point arguments.

Acknowledgments
This work was supported by the project MSM4781305904 of the Czech Ministry of Education.

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