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STABLE, CHAOTIC AND OPTIMAL SOLUTIONS OF FIRST ORDER PARTIAL DIFFERENTIAL EQUATIONS RELATED WITH THE CELL KINETICS

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1. Introduction

The purpose of this lecture is to show that the dynamical systems described by some simple first order partial differential equations may have a complicated behavior. This is in particular true for the equation

$$\frac{\partial u}{\partial t} + c(t,x)\frac{\partial u}{\partial x} = f(t,x,u) \qquad \text{for} \quad (t,x) \in D \tag{1}$$

considered with the initial value condition

$$u(0,x) = v(x) \qquad \text{for} \quad x \in \Delta . \tag{2}$$

Here $\Delta = [0,L]$, $D = [0,\infty) \times \Delta$ and c,f are given continuously differentiable functions satisfying

$$c(t,x) \geqslant 0 \tag{3_I}$$

$$f(t,x,u) \leqslant k_1(t)u + k_2(t), \qquad f(t,x,0) \geqslant 0 \tag{3_{II}}$$

with continuous coefficients k_1, k_2 .

Equation (1) has an interesting biological application [7] . It may be used to describe the growth of a population of cells which constantly differentiate (change their properties) in time. In this model t denotes the time and x is the degree of the differentiation which changes from $x = 0$ (undifferentiated cells) to $x = L$ (mature cells). The unknown function $u(t,x)$ is the distribution of cells with respect to the parameter x. Thus, roughly speaking, $u(t,x)\,dx$ is the number of cells having at time t the degree of differentiation between x and $x + dx$. The coefficient c is the velocity of the cell differentiation and the right hand side f is related with the reproduction of cells. Since the process of the differentiation is, in general, irreversible, this interpretation justifies inequality (3_I). Inequalities (3_{II}) follow from the fact that the proliferation rate is always bounded and that the number of cells cannot decrease if there is no cells.

Denote by $C_+(\Delta)$ and $C_+(D)$ the space of all non-negative functions continuous and defined on the interval Δ and the domain D respectively. A function $u \in C_+(D)$ will be called a generalized solution of (1) if there is a sequence $\{u_n\}$ of continuously differentiable functions in D satisfying (1) and such that $\{u_n\}$ converges to u uniformly on compact subsets of D. We shall consider only generalized solutions and the word "generalized" will be omitted. Using the method of characteristics it is easy to prove the following

<u>Proposition 1</u>. Suppose that c and f satisfy inequalities (3). If, in addition, c satisfies condition

$$(4) \qquad c(t,0) = 0 \qquad \text{for} \quad t \geqslant 0,$$

then for every $v \in C_+(\Delta)$ problem (1),(2) has a unique solution $u \in C_+(D)$; conversely if for one $v \in C_+(\Delta)$ problem (1),(2) has a unique solution $u \in C_+(D)$, then c satisfies (4).

The singularity condition (4) causes some specific properties of equation (1) such as the existence of stationary turbulent solutions [6] in the sense of J.Bass [2] and the existence of an ergodic invariant measure in the phase space [3] . From the biological point of view it means that the primitive, undifferentiated cells change their properties slowly.

2. <u>Stability</u>

From now we shall consider the autonomous equation

$$(5) \qquad \frac{\partial u}{\partial t} + c(x)\frac{\partial u}{\partial x} = f(x,u) \qquad \text{for} \quad (t,x) \in D.$$

We admit, as usual, that c and f are continuously differentiable and we shall assume that

$$(6_I) \qquad c(0) = 0, \qquad c(x) > 0 \quad \text{for} \quad 0 < x \leq L$$

$$(6_{II}) \qquad f_u(0,u_0) < 0, \qquad f(0,u)(u - u_0) < 0 \quad \text{for } u > 0,\ u \neq u_0$$

$$(6_{III}) \qquad f(x,u) \leqslant k_1 u + k_2, \qquad 0 = f(x,0) \quad \text{for} \quad x \in \Delta\ ,\ u \geqslant 0$$

with constant k_1, k_2 and $u_0 > 0$. We have the following [4]

<u>Theorem 1</u> . Suppose that c and f satisfy condition (6). Then there exists a unique function $w_0 \in C_+(\Delta)$ such that

$$(7) \qquad \lim_{t \to \infty} u(t,x) = w_0(x) \qquad \text{uniformly for } x \in \Delta$$

for every solution $u \in C_+(D)$ of (5) satisfying $u(0,0) > 0$.

Observe that in the statement of Theorem 1 there is no assumption (except the growth condition (6_{III})) concerning the behavior of $f(x,u)$ for $x > 0$. On the other hand the existence of the limit (7) is claimed for all $x \in \Delta$. Again, this fact has an immediate biological interpretation. For the stability of a self-maintaining cell population only the conditions for the basic, undifferentiated cells are essential.

3. Chaos

Let V be a metric space and let $\{S_t\}$ $(t \geq 0)$ be a semidynamical system on V, i.e. S_t are continuous mappings from V into itself satisfying

$$S_0 = id_V \quad , \quad S_{t+t'} = S_t \circ S_{t'} \qquad \text{for } t,\ t' \geq 0.$$

A point $v \in V$ is called stable if for any sequence $\{v_n\} \subset V$ the condition $v_n \to v$ implies $S_t v_n \to S_t v$ (as $n \to \infty$) uniformly for all $t \geq 0$. The system $\{S_t\}$ is called chaotic if the following [1] two conditions are satisfied:

(a) every point $v \in V$ is unstable (= it is not stable),

(b) there exists $v \in V$ such that the trajectory $\{S_t v:\ t \geq 0\}$ is dense in V.

Now let $\{S_t\}$ be the semidynamical system on $C_+(\Delta)$ generated by initial value problem (5),(2); that is $(S_t v)(x) = u(t,x)$ where u is the solution of (5),(2). Under conditions (6) the subsets of $C_+(\Delta)$ defined by

$$V_+ = \{v \in C_+(\Delta):\ v(0) > 0\} \ , \quad V_0 = \{v \in C_+(\Delta):\ v(0) = 0\}$$

are evidently invariant ($S_t V_+ \subset V_+$ and $S_t V_0 \subset V_0$ for $t \geq 0$). The behavior of $\{S_t\}$ on V_+ is described by Theorem 1. The behavior of $\{S_t\}$ on V_0 is much more complicated. An important role is played here by the set

$$V_w = \{ v \in V_0:\ v(x) < w_0(x) \text{ for } x \in \Delta\}$$

which is a global atractor.

Theorem 2. Suppose that c and f satisfy (6) and let $\{S_t\}$ be the semidynamical system generated by (2),(5). Then for each $v \in V_0$ there is a time $T_0 \geq 0$ such that $S_t v \in V_w$ for $t \geq T_0$. The set

V_w is invariant under $\{S_t\}$ and $\{S_t\}$ restricted to V_w is chaotic.

The proof of the last statement in Theorem 2 is not trivial and will be published in [4]. Biological interpretation of Theorem 2 leads to the following conclusion: if the basic cells are damaged, then the behavior of the total population is unpredictable.

4. Optimal control

The most interesting property of equation (1) is related with the fact that the coefficient c (and partially also f) may be considered as a control factor. An important, from the applied point of view [5], problem may be formulated as follows. Assume that $c(t,x) = r(t)x$ and $f(t,x,u) = [\lambda(1-u) - r(t)]u$. Given $v \in C_+(\Delta)$ ($v(x) \leqslant 1 - 1/\lambda$) find a function $r(t) \in [0,1]$ for which the integral

$$I(r) = \int_0^l r(t)u(t,L)\,dt$$

admits its maximal value. The optimal function r corresponds to the most effective treatment of some cases of anemia. Such a treatment, based on theoretical conclusions, has been tried on number of patients by Dr. M. Ważewska-Czyżewska with success.

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