Mimmo Iannelli (Ed.)

Mathematics of Biology

80

Cortona, Italy 1979







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Lectures given at a Summer School of the Centro Internazionale Matematico Estivo (C.I.M.E.), held in Cortona (Arezzo), Italy, June 18-30, 1979





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ISBN 978-3-642-11068-9 e-ISBN: 978-3-642-11069-6

DOI:10.1007/978-3-642-11069-6

Springer Heidelberg Dordrecht London New York

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CENTRO INTERNAZIONALE MATEMATICO ESTIVO (C.I.M.E.)

DELAY DIFFERENTIAL EQUATIONS

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DELAY DIFFERENTIAL EQUATIONS

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1. Introduction

The purpose of these lectures is to survey parts of the theory of delay-differential equations and functional differential equations that have been used or may be used in the modeling of biological phenomena. In the course of doing so, reference will be made from time to time to specific applications in biology, but primarily to illustrate the mathematical techniques. No attempt will be made to survey comprehensively any particular field in biology, since other lecturers here are doing so. We shall try to begin with elementary concepts of the theory, and yet to present some of the most recent results.

In the first lecture, I shall first indicate a few biological problems that give rise to delay differential equations, and give a large number of references. Then, since some of the audience may have only a slight acquaintance with such equations, I shall sketch their fundamental theory.

Standard notations will be introduced and classifications of the equations into types (retarded, neutral, finite or infinite delay, etc.) will be described. Basic existence, uniqueness, continuation, and continuity theorems will be briefly described.

Because of limitations of time and space, it is impossible to mention all aspects of the subject, for which the extant literature now includes thousands of papers. We shall attempt to select aspects of the greatest usefulness from the viewpoint of the applications in biology. Nor, of course, is there room to supply proofs for more than a handful of theorems. It is hoped that interested readers can make up for these shortcomings by consulting the substantial list of references supplied, and exploring other literature.

Chapter II of these lectures (Sections 7-9) will develop the theory of linear autonomous retarded functional differential equations, emphasizing the semigroup and spectral theory. This will be done for equations with finite delay, with brief mention of analogous theories for infinite delays. Also in this chapter is a sketch of the use of the Laplace transform, and a theorem on stability by linearization.

In Chapter III, I shall discuss the exponential polynomials that arise from the characteristic equations associated with functional differential equations. The problem to be discussed is that of determining stability or instability. Our brief treatment includes recent criteria of Datko.

Chapter IV (Sections 11 and 12) is devoted to Liapunov stability theory, including the invariance principle. Also, we shall present some of the recent work of Infante, Walker, and Carvalho on the existence and form of best Liapunov functionals.

Chapter V is on the existence of periodic solutions. I shall discuss the method of ejective fixed point theory, illustrating the theory with recent work of Banks, Mahaffy, and others, on biochemical oscillators and population models.

Sections are numbered consecutively through these lectures, and equations and theorems are numbered consecutively within each section. For example, Equation (7.2) is the second numbered equation in Section 7. References are collected at the end in alphabetical order.

The author wishes to thank the organizers of this C.I.M.E. meeting for the opportunity to present these lectures. Also, he thanks Stavros Busenberg for reading these notes and making several helpful suggestions, and he wants to express his appreciation to the Applied Mathematics Division of Brown University for its hospitality during a sabbatical leave in 1978-79.

CHAPTER I. BASIC CONCEPTS

2. Sources of delay differential equations in biology

Ordinary differential equations or systems can usually be taken in the form (\dot{x} denotes dx/dt)

$$\dot{x}(t) = f(t,x)$$

and the basic problem is to determine or describe the solutions, meaning functions $\mathbf{x}(\mathsf{t})$ that satisfy

$$\dot{x}(t) = f(t,x(t))$$

The simplest delay differential equations are of the form

(2.1)
$$\dot{x}(t) = f(t,x(t),x(t-r))$$

where r is a positive constant, or a given function of t. The basic problem is to determine or describe functions x(t) with the property that

when in f(t,x,y) we replace x by the function x(t) and y by the shifted function x(t-r), we obtain dx(t)/dt. More generally and somewhat vaguely, we might consider equations of the form

$$\dot{x} = f(t,x(t),x(\cdot))$$

where by $x(\cdot)$ we mean the values of x over some t-interval, for example [t-r,t] or $(-\infty,t)$. That is, f is a functional on x. Such equations were called hereditary differential equations by V. Volterra.

Equations of these kinds have been used by many authors in the description of physical and biological processes. For example, in the theory of population dynamics of a single species, the basic equation for the size of the population at time t, N(t), is $\dot{N}(t)$ = births minus deaths (per unit time). In the simplest linear model, one assumes that births and deaths are a fixed proportion of N(t), thus $\dot{N}(t)$ = bN(t) - dN(t). However, assuming a finite constant gestation time r, we get $\dot{N}(t)$ = bN(t-r) - dN(t). This is a linear equation of the form (2.1). More generally, one can postulate nonlinear birth rates and death rates, obtaining

$$\dot{N}(t) = f(N(t-r))N(t-r) - g(N(t))N(t)$$

where f and g are suitable functions. For discussions of population growth models under various assumptions, see Perez et al (1978), Cushing (1976, 1977), Cooke and Yorke (1973), Brauer (1977), and so on, including the C.I.M.E. lectures here by Professor Cushing.

The famous prey-predator model of Lotka and Volterra has been generalized to include time delays. In fact, Volterra himself formulated such a model under the assumption that the growth benefit to predators of contact with prey is not instantaneous, due for example to a gestation period. Volterra's model is

$$\dot{N}_{1}(t) = N_{1}(t)[b_{1}-a_{1}N_{2}(t)]$$

$$(2.2)$$

$$\dot{N}_{2}(t) = N_{2}(t)[-b_{2}+a_{2}\int_{-\infty}^{t} N_{1}(s)k(t-s)ds]$$

where k(t) is a kernel function that is supposed to describe the way in which the present gain to the predator depends on the past size of the prey population N_1 . For discussion of prey-predator and competition models with delays, the reader may refer to Ladde (1976), Cushing, Leung (1977, 1979), MacDonald (1976, 1977, 1978), May (1973), and Hastings (1977).

Delay equations also arise in the mathematical theory of epidemics, because of the incubation periods or maturation periods of the bacteria, viruses, and parasites that cause illness. For some recent work of this kind, see Cooke and Yorke (1973), Hoppensteadt (1975), Cooke (1979), Busenberg and Cooke (1978, 1979), Grossman (1978), Hethcote, Stech, and van den Driessche (1979).

Similarly, delay equation models have been devised to describe the production of blood cells, the delays arising because of the time required for maturation of cells or transformation of one kind of cell to another. In these models, one has to simplify by assuming that there is a small finite number of distinct types of cells, and a well-defined time at which a given cell changes to a different type. The time delay models are thus in a certain sense approximate equations replacing a much larger and more complicated set of equations (not actually known, perhaps) that more accurately embody the physiology and chemistry of the system. For recent work on blood models, see Glass and Mackey (1977), Rubinow and Lebowitz (1975), Wheldon (1975), MacDonald (n.d.), Martelly, Schmitt, and Smith (n.d.).

Mention should also be made of models describing metabolic or biochemical systems in organisms. Time delays may be incorporated because of the finite time required to complete such processes as transcription or translation of genes, and again one should probably think of these models as convenient

approximations to very complex processes. For the most recent work see Banks and Mahaffy (1978), Mahaffy (1979), and the references therein. In a later section we will describe this work in more detail.

Mathematical immunology is a rapidly developing area, and a number of models using delay differential equations have been formulated. The delays may be postulated to arise because of the time required for the immune system to respond to an antigen, or because a certain threshold of antigen must be attained before the immune system is activated. See Waltman and Butz (1977), Grossman (n.d.). Also, delay differential equations have been employed by S. Grossberg (1967, 1968a, b) as models in prediction and learning theory.

3. The class of equations considered

From the few examples already given, it is clear that a wide variety of equations arise from biological models with some kind of hereditary effect. We want to examine a mathematical theory that is sufficiently general to include many or most of these, yet is capable of fruitful specialization to particular cases. At a minimum, we want to include differential-difference equations such as

(3.1)
$$\dot{x}(t) = g(t,x(t),x(t-r),...,x(t-r_m))$$

where r_1, r_2, \ldots, r_m are positive constants and $x \in \mathbb{R}^n$ (see Bellman and Cooke (1963)), and delay-differential equations, which we think of as having the same form but possibly with r_1, r_2, \ldots, r_m being given functions of t. However, Eq. (3.1) is not always realistic as a model, because it implies that the delayed effects occur at discrete time delays r_1, r_2, \ldots, r_m . In many cases, it appears to be more realistic to assume that the delayed effect

is "smeared out" over a time interval, or in other words that there is a distributed delay, similar to that in Eq. (2.2). In this way one is led to consider integro-differential-delay equations.

A class of equations permitting quite general delayed effects, for which extensive theoretical development now exists, is the class of <u>functional</u> <u>differential equations</u>, as defined by Hale (1971, 1977). Suppose that $r \ge 0$ is a given real number, $R = (-\infty, \infty)$, n is a positive integer, and $C = C([-r,0],\mathbb{R}^n)$ is the Banach space of continuous functions defined on the interval [-r,0] with values in \mathbb{R}^n , with the usual supremum norm. Let $\sigma \in \mathbb{R}$, A > 0, and let $x \in C([\sigma-r,\sigma+A],\mathbb{R}^n)$. For any $t \in [\sigma,\sigma+A]$, let x_+ denote the element of C defined by

$$x_{t}(\theta) = x(t+\theta), \quad \theta \in [-r,0].$$

That is, x_t denotes the "section of x" that lies over the interval [t-r,t], regarded as an element in the function space C. Now let $f:D \to \mathbb{R}^n$ be a given function with domain D lying in $\mathbb{R} \times \mathbb{C}$. The equation

$$\dot{x}(t) = f(t,x_t)$$

(where the dot denotes the right-hand derivative) is called a retarded functional differential equation with finite delay. Sometimes we shall denote this equation by RFDE or RFDE(f). The idea of this equation is that if $x(\cdot)$ is known on the interval [t-r,t], then $\dot{x}(t)$ is known, and so we should be able to continue x as a solution of the equation to the right of t. In fact, we can define a function x to be a solution of RFDE(f) on $[\sigma-r,\sigma+A]$ provided:

(i)
$$x \in C([\sigma-r,\sigma+A],\mathbb{R}^n)$$

(ii)
$$(t,x_t) \in D$$
, for $t \in [\sigma,\sigma+A)$

(iii) x(t) satisfies (3.2) for t ∈ [σ,σ+A).

Eq. (3.1) is a special case of Eq. (3.2) obtained when the function $f(t,\phi)$, for $\phi \in C([-r,0],\mathbb{R}^n)$, has the form

$$f(t,\phi) = g(t,\phi(0),\phi(-r),...,\phi(-r_m))$$

since $x_t(-r_j) = x(t-r_j)$, j = 0,1,...,m. Eq. (3.2) also includes various integro-differential equations. For example, if we take f of the form

$$f(t,\phi) = g(t,\phi(0)) + \int_{-r}^{0} k(t,s,\phi(s))ds$$

then Eq. (3.2) reduces to

(3.3)
$$\dot{x}(t) = g(t,x(t)) + \int_{-r}^{0} k(t,s,x(t+s))ds.$$

Thus, Eq. (3.2) is very general and includes many cases of interest in the applications. Moreover, an adequate theory of stability and oscillation, even for simpler equations such as Eq. (3.1), is best carried out in the context of the theory of infinite-dimensional spaces, and in this context Eq. (3.2) can in many respects be handled conveniently. Therefore, we shall take RFDE(f) as the basic object for discussion in these lectures.

Certain extensions of Eq. (3.2) will also be considered from time to time. In the first place, there is a question as to the correct space in which to take the elements \mathbf{x}_t and certain alternatives to C[-r,0] will be mentioned subsequently. Also, one may object to the restriction to a finite delay, especially because Eq. (3.2) does not naturally include Volterra-type equations such as

$$\ddot{x}(t) = g(t,x(t)) + \int_{0}^{t} K(t,s,x(s))ds$$

or

$$\dot{x}(t) = g(t,x(t)) + \int_{-\infty}^{t} K(t,s,x(s))ds.$$

In order to include such equations in the form (3.2), ony may re-define the symbol \mathbf{x}_{\downarrow} by

$$x_{t}(\theta) = x(t+\theta) \quad \theta \in (-\infty,0]$$

An equation of the form (3.2) may then be called an RFDE with infinite or unbounded delay. In this case, it is not as easy to choose an appropriate function space in which to imagine that the elements \mathbf{x}_t lie. We shall comment on this and give a number of references in Section 6, but for the most part our lectures will concentrate on equations with finite or bounded delay.

Another class of some interest is the class of <u>neutral</u> equations. Neutral differential-difference equations have the form

$$\dot{x}(t) = g(t,x(t-r_1),...,x(t-r_m),\dot{x}(t),...,\dot{x}(t-r_m)).$$

The implicit way in which $\dot{x}(t)$ enters here can cause difficulties, and more special forms such as

(3.4)
$$\frac{d}{dt} [x(t) - \sum_{j=1}^{m} c_{j}x(t-r_{j})] = g(t,x(t),x(t-r_{1}),...,x(t-r_{m}))$$

may be preferred. A general class of neutral functional differential equations of the form

$$\frac{d}{dt} D(t,x_t) = f(t,x_t)$$

is treated in Hale (1977), under suitable conditions on the function D. Since the theory of these equations is a little more complicated, and they have so far found few applications in biology, we shall not set forth this theory here. Also, it should be noted that if we take g=0 in Eq. (3.4) and integrate, we obtain a pure difference equation (in which the delays r_1, \ldots, r_m are not necessarily commensurable). Thus, neutral FDE's in a certain sense encompass difference equations, which of course are widely used in biology.

Finally, we wish to mention more general FDE's of the form (3.2) in which

 $\mathbf{x}(t)$ has values lying, not in \mathbb{R}^n , but in more general Banach or Hilbert spaces. The advantage of this generality is that it permits the consideration of certain partial differential equations with delays, which can arise for example in diffusion problems. This is an area of recent development, and will not be discussed here. See, for example, Travis and Webb (1974, 1976, 1978).

4. The initial value problem

It is easy to formulate a well-posed initial value problem for the differential-difference equation (3.1). Assume that $0 < r_1 < r_2 < \ldots < r_m$ and for convenience let $r = r_m$ and $r_o = 0$. Let t_o be an <u>initial point</u> and let ϕ be an <u>initial function</u> given on the <u>initial interval</u> $[t_o - r, t_o]$. Assume that ϕ is continuous and that $g(t, x, x_1, \ldots, x_m)$ is a given continuous function of all its variables. Then the initial value problem IVP is to solve Eq. (3.1) on $t \ge t_o$ subject to the condition

(4.1)
$$x(t) = \phi(t), \quad t \in [t_0 - r, t_0].$$

Now for $t - t_0 \le r_1$, Eqs. (3.1) and (4.1) imply

$$\dot{x}(t) = g(t,x(t),\phi(t-r),...,\phi(t-r_m))$$

$$x(t_0) = \phi(t_0).$$

Thus, the problem is reduced to an IVP for an ordinary differential equation on $t_0 \le t \le t_0 + r_1$. All the usual theorems on existence, uniqueness, and continuous dependence on $t_0, \phi(t_0)$, and g can be applied. Further, if we assume that a solution x(t) exists for $t \in [t_0, t_0 + r_1]$, then Eq. (3.1)

implies that for $t_0+r_1 \le t \le t_0+\min(2r_1,r_2)$ we have

$$\dot{x}(t) = g(t,x(t),x(t-r_1),\phi(t-r_2),...,\phi(t-r_m))$$
.

Requiring x(t) to be continuous at $t = t_0 + r_1$, we again have an IVP for an ordinary differential equation (since $x(t-r_1)$ is known), and again the usual theorems can be applied. By this step-by-step process, a solution of Eq. (3.1) can be produced corresponding to any given continuous initial function ϕ . For a more general discussion of this method of steps, see El'sgol'ts and Norkin (1973). One of the main things to note from this discussion is that the solution composed of ϕ and its extension x is continuous wherever it exists, and c^1 for $t > t_0$, but in general not differentiable at t_0 (although the right-hand derivative exists). Moreover, if g is smooth, then $x \in c^2$ for $t > t_0 + r_m$. Thus, a solution tends to become smoother as t increases.

The method of steps is not applicable to the general RFDE, and existence results are generally obtained by applying fixed point theorems. For equations with finite delay and continuous initial data, the basic IVP consists of Eq. (3.2) coupled with the initial datum

$$x(t_0+\theta) = \phi(\theta), \quad \theta \in [-r,0]$$

where ϕ is a given function in $C = C([-r,0],\mathbb{R}^n)$. The initial condition can be simply expressed in the form $x_{t_0} = \phi$. In order to have a shorter notation, we shall often use σ instead of t_0 as the initial point, so the IVP is

(4.2)
$$\dot{x}(t) = f(t, x_t), \quad t \ge \sigma$$

$$x_{\sigma} = \phi .$$

The following theorems have been proved (Hale (1977)).

Existence Theorem. Suppose Ω is an open subset in $\mathbb{R} \times \mathbb{C}$ and $f^O \in C(\Omega,\mathbb{R}^n)$. If $(\sigma,\phi) \in \Omega$, then there is a solution of Eq. (4.2) with $f = f^O$. More generally, let W be a compact subset of Ω and $f^O \in C(\Omega,\mathbb{R}^n)$. Then there is a neighborhood $V \subseteq \Omega$ of W such that f^O is continuous and bounded on V, and there is a neighborhood $V \cap \mathbb{R}^n$ in the space of bounded continuous functions on V into \mathbb{R}^n , and an $\alpha > 0$, such that for any $(\sigma,\phi) \in W$ and any $f \in U$ there is a solution $x \in x(\sigma,\phi,f)$ of RFDE(f) with initial condition (σ,ϕ) which exists on $[\sigma-r,\sigma+\alpha]$.

Uniqueness Theorem. Suppose Ω is an open subset in $\mathbb{R} \times \mathbb{C}$, $f \in C(\Omega, \mathbb{R}^n)$ and f satisfies a Lipschitz condition in ϕ in each compact set in Ω . That is, for any compact set K in Ω , there is a constant $\alpha = \alpha(K)$ such that

$$|f(t,\phi) - f(t,\psi)| \leq \alpha |\phi - \psi|$$

for $(t,\phi)\in K$, $(t,\psi)\in K$. Then for any $(\sigma,\phi)\in \Omega$, there is a unique solution of Eq. (4.2).

A solution of Eq. (4.2) will sometimes be called a solution of $\dot{x} = f(t, x_t)$ through (σ, ϕ) , and denoted by $x(\sigma, \phi)$ or $x(\sigma, \phi, f)$. We point out that in the Lipschitz condition, we are using the vertical bars $|\cdot|$ to denote the norm in \mathbb{R}^n on the left and the norm in \mathbb{C} on the right.

Also available is a theorem showing the continuous dependence over a finite time interval of the solution $x(\sigma,\phi,f)$ on (σ,ϕ,f) in the sense that if $\{\sigma^k\}$, $\{\phi^k\}$, $\{f^k\}$ are sequences and $\sigma^k \to \sigma$, $\phi^k \to \phi$, $f^k \to f$ in the appropriate norms, then $x(\sigma^k,\phi^k,f^k) \to x(\sigma,\phi,f)$ on $(\sigma-r,\sigma+A]$. Moreover, theorems on the maximal interval of existence, and on differentiability properties of solutions, are known.

One important way in which the theory of the RFDE differs from the theory of ordinary differential equations is that, in general, <u>backward continuation</u> of a solution is not possible. For an ordinary DE, $\dot{x}(t) = f(t,x(t))$, if

 (t_0,x_0) is an initial point and f is continuous in a neighborhood of (t_0,x_0) , then a solution x(t) will exist on an interval $(t_0-\delta,t_0+\delta)$, $\delta>0$. On the other hand, for the RFDE with initial data (σ,ϕ) there may be a solution x satisfying Eq. (3.2) for $\sigma \leq t < \sigma + A$, but it may not be possible to extend x to the left of σ -r in such a way that Eq. (3.2) is satisfied for $\sigma-\epsilon \leq t < \sigma + A$, no matter how small ϵ is. Indeed, it is clearly necessary that ϕ be diffierentiable on $(-\epsilon,0]$ for this to be so. Thus, the RFDE has the important property of imposing a preferred direction to the variable t. For further discussion of the backward continuation problem, see Hastings (1969), or Hale (1977).

5. Operator of translation along trajectories

Many important results in the theory of FDE's are based on the concept of the orbit or trajectory of an equation. Consider the initial value problem

$$\dot{x}(t) = f(t, x_t)$$

$$x_0 = \phi$$

and assume that there is a unique solution $x(t) = x(\sigma, \phi, f)(t)$. For each $t \ge \sigma$, we may consider the element x_t lying in the space C. Define the operator

$$T(t,\sigma): C \to C$$

 $T(t,\sigma)\phi = x_t(\sigma,\phi,f)$

That is, for a given equation, a given σ and given $t \geq \sigma$, $T(t,\sigma)$ is the operator which associates to each ϕ the solution segment x_t emanating from the initial condition ϕ at time σ . This is analogous to the idea,

for ordinary differential equations, of regarding the equation as generating a flow on the phase space \mathbb{R}^n . In our case, the <u>phase space</u> is the infinite-dimensional space C. The operator $T(t,\sigma)$ is called the <u>solution map</u> or the <u>operator of translation along trajectories</u>. Moreover, in analogy to the situation for ordinary DE's, we call the set

$$\{x_t(\sigma,\phi,f): \sigma \leq t < \infty\}$$

the positive semi-orbit through (σ,ϕ) , assuming that x_t exists over $[\sigma,\infty)$.

Throughout the rest of this section we assume that $T(t,\sigma)$ exists for $t \geq \sigma$. The operator $T(t,\sigma)$ has many interesting properties. One that is particularly important arises from the observation that if f is continuous, then since x(t) will be continuous in t, the function $\dot{x}(t)$ will be continuous for $t \geq \sigma$, hence $x(t+\theta)$ will be continuously differentiable with respect to θ for $t \geq \sigma+r$, $\theta \in [-r,0]$. This makes it possible to derive a compactness result for $T(t,\sigma)$; one way to state this is as follows:

$$(S(t)\phi)(\theta) = \begin{cases} \phi(t+\theta) - \phi(0), & t+\theta < 0 \\ 0 & t+\theta \ge 0 \end{cases}$$

where $-r \le \theta \le 0$, $t \ge 0$. Thus, $S(0)\phi$ is ϕ minus the constant $\phi(0)$, and $S(t)\phi$ is obtained by extending $\phi-\phi(0)$ as the zero function to the right of zero. S(t) is a bounded linear operator on C for each $t \ge 0$ and satisfies

$$S(t+\tau) = S(t)S(\tau), \quad t \ge 0, \quad \tau \ge 0$$

 $S(t) = 0, \quad t \ge r$

Theorem 5.1. If $f: \mathbb{R} \times \mathbb{C} \to \mathbb{R}^n$ is a bounded continuous map and if

 $T(t,\sigma):C \to C$ is a map bounded uniformly for t in each compact subset of $[\sigma,\infty)$, then

$$T(t,\sigma) = S(t-\sigma) + U(t,\sigma), \quad t \ge \sigma$$

where $U(t,\sigma)$ is, for each $t \ge \sigma$, completely continuous. In particular, $T(t,\sigma)$ is completely continuous for each $t \ge \sigma + r$. (Hale, (1977)).

6. Equations with unbounded delay

For functional differential equations of retarded type with finite delay r, the solution operator $T(t,\sigma)$ for each $t \ge \sigma + r$ is completely continuous, under weak hypotheses on f. In other words, the operator T has a smoothing or compactifying property. This makes it possible (see Chapter II) to obgain complete complete information about the spectral properties for linear equations and to construct a satisfying general theory.

By an RFDE with unbounded delay or infinite delay, we mean an equation of the form

(6.1)
$$\dot{x}(t) = f(t, x_t), \quad t \ge \sigma$$

where now x_t is a symbol for the entire "history" of the function x on $(\sigma,t]$, or on $(-\infty,t]$, and f must be defined on some set of these histories. For example, two equations of this kind are

$$\dot{x}(t) = x(\frac{t}{2}), \quad t \ge 0$$

$$\dot{x}(t) = g(x(t-r)) + \int_{-\pi}^{0} b(\theta)x(t+\theta)d\theta, \quad t \ge 0$$

where, in the first case, $f(t,\phi) = \phi(-t/2)$.

For these equations, there is some difficulty in choosing or defining a suitable "phase space" of functions. For equations with finite delay, this choice is not critical for most purposes, because usually one wants to consider x(t) continuous for $t \ge \sigma$. Then x_{t} will be continuous in t for $t \ge \sigma + r$ and $\dot{x}(t)$ will be continuous for $t \ge \sigma + r$. Thus, C or c^1 may be chosen as the phase space. However, for equations with infinite delay, \mathbf{x}_{\downarrow} always includes all the initial data ϕ and consequently is never smoother than \$\phi\$ itself. Several different spaces have been suggested as appropriate phase spaces. Recently, Hale and Kato (1978) and Schumacher (1978) have set down very general axioms that include many specific possibilities and have deduced a general theory from these axioms. In this way, they have explored ramifications of different choices. For want of space, we shall not discuss equations with infinite delay further. Also, in most biological applications, it is reasonable to assume finite delays. For additional information and references on unbounded delay, refer to the survey paper by Corduneanu and Lakshmikantham (1979).

CHAPTER II. AUTONOMOUS LINEAR FUNCTIONAL DIFFERENTIAL EQUATIONS

7. Linear autonomous systems and semigroups

A linear autonomous RFDE is of the form

$$\dot{x}(t) = L(x_t)$$

where L is a continuous linear map. In this Chapter attention is restricted to the case of finite delay, and primarily to the case in which L maps $C = C([-r,0],\mathbb{R}^n)$ into \mathbb{R}^n . Since L is linear, it has a representation

(7.2)
$$L(\phi) = \int_{-r}^{0} [d\eta(\theta)]\phi(\theta), \quad \phi \in C$$

where n is an n by n matrix-valued function of bounded variation on [-r,0]. In this section, I shall show that the solution operator T(t) gives a semigroup of linear transformations on C, and will characterize the infinitesimal generator of this semigroup and its spectrum. Exponential bounds on solutions in terms of the spectrum, or roots of the characteristic equation, are obtained, and these form the basis for linear stability theory. In addition, general theorems of functional analysis imply that the space C can be split into a direct sum of a finite dimensional space corresponding to the roots of large real parts and another space corresponding to roots with smaller real parts. Such a splitting is important in the general qualitative theory of FDE's, but will be employed in these lectures only in Section 13 on the method of ejective fixed points. Also in this section I state a

variation of constants formula for nonhomogeneous systems, and refer to extensions valid in other phase spaces.

Section 8 briefly describes an explicit representation formula for solutions, and the Laplace transform method for deriving it. Section 9 presents a theorem justifying the method of linearization in analyzing the (local) stability of an equilibrium point of a nonlinear autonomous equation.

Let $\phi \in C$ and let $x = x(\phi)$ be the unique solution of Eq. (7.1) for $t \ge 0$ satisfying the initial condition $x_0 = \phi$. Define $T(t):C \to C$ by $T(t)\phi = x_t(\phi)$. T(t) is the solution operator or operator of translation along trajectories.

Lemma 7.1. For each $t \ge 0$, T(t) is a bounded linear operator on C. The family $\{T(t)\}$, $t \ge 0$, is a semigroup of bounded linear operators, that is, it satisfies:

(i)
$$T(0) = I$$

(ii)
$$T(t+\tau) = T(t)T(\tau)$$
 for all $t \ge 0$, $\tau \ge 0$

(iii) T(t) is strongly continuous, that is, for all $t \geq 0, \quad \phi \in C,$

$$\lim_{\tau \to t} |T(t)\phi - T(\tau)\phi| = 0$$

Furthermore, for each $t \ge r$, T(t) is completely continuous (compact); that is, T(t) is continuous and maps bounded sets into relatively compact sets.

<u>Proof.</u> The semigroup property follows from uniqueness of solution since $T(t+\tau)\phi$ and $T(t)T(\tau)\phi$ are both solutions, as a function of t, with the same initial condition $T(\tau)\phi$. By definition, T(0) = I. From the definition of L, $|L(\phi)| \le v|\phi|$ where v is the total variation of η . For any $t \ge 0$ and $-r \le \theta \le 0$,

(7.3)
$$T(t)\phi(\theta) = \phi(t+\theta) \quad \text{if} \quad t+\theta \le 0$$

$$= \phi(0) + \begin{cases} t+\theta \\ 0 \end{cases} L(T(s)\phi)ds, \quad \text{if} \quad t+\theta > 0.$$

Hence

$$\left|\mathbf{x}_{t}\right| = \left|\mathbf{T}(t)\phi\right| \leq \left|\phi\right| + \int_{0}^{t+\theta} \left|\mathbf{L}(\mathbf{T}(s)\phi)\right| ds \leq \left|\phi\right| + v \int_{0}^{t} \left|\mathbf{T}(s)\phi\right| ds.$$

From Gronwall's inequality we now get

$$|T(t)\phi| \leq |\phi|e^{Vt}$$

and therefore T(t) is bounded. To show that T(t) is strongly continuous, we need only show that $\lim_{t\to 0+} |T(t)\phi-\phi|=0$ (since T has the semigroup that T(t)) property). This is clear from the equation for $T(t)\phi(\theta)$. To show that T(t) is compact for $t\geq r$, consider any bounded set $S=\{\phi\in C: |\phi|\leq K\}$. For any $\psi\in T(t)S$, $t\geq r$, we have $\psi=T(t)\phi=x_t$ where $x=x(\phi)$. So

$$|\psi| = |T(t)\phi| \le |\phi|e^{vt} \le Ke^{vt}$$
.

From the equation itself, $|\dot{x}(t)| \le v|x_t| \le vKe^{vt}$. Therefore the set T(t)S is uniformly bounded and equicontinuous and, by the Ascoli-Arzela theorem, contained in a compact set of C.

Recall that if $\{T(t), t \ge 0\}$, is a strongly continuous semigroup of linear operators on C, the infinitesimal generator of T(t) is the operator A:C \rightarrow C,

(7.4)
$$A\phi = \lim_{t\to 0+} \frac{1}{t} [T(t)\phi - \phi]$$

where the domain of A, D(A), is the set of ϕ where this limit exists. The following are known properties of strongly continuous linear semigroups.

- (1) D(A) is dense in C.
 - (2) If $\phi \in D(A)$ then

(7.5)
$$\frac{d}{dt} T(t)\phi = T(t)A\phi = AT(t)\phi.$$

Since $T(t)\phi = x_t(\phi)$ in our case, this implies validity of the evolution equation

(7.6)
$$\frac{d}{dt} x_t = Ax_t \text{ for } \phi \in D(A).$$

- (3) If $\mu(t)$ is in the point spectrum $P\sigma(T(t))$, and $\mu(t) \neq 0$, then there is a λ in the point spectrum $P\sigma(A)$ such that $\mu(t) = e^{\lambda t}$. Conversely, if $\lambda \in P\sigma(A)$, then $e^{\lambda t}$ is in $P\sigma(T(t))$. Briefly, $P\sigma(T(t)) = e^{tP\sigma(A)}$ plus possibly $\{0\}$.
- (4) Suppose that for some $\tau > 0$, the spectral radius $\rho(T(\tau)) \neq 0$. Let $\beta = (\log \rho)/\tau$. For any $\epsilon > 0$ there is a constant $K(\epsilon) \geq 1$ such that

(7.7)
$$|T(t)| \le K(\varepsilon)e^{(\beta+\varepsilon)t}$$
, for all $t \ge 0$, $\phi \in C$.

Eq. (7.7) and (3) show that the rate of growth of |T(t)| is controlled by $P\sigma(A)$.

We shall show that A can be calculated explicitly in the present case. For $\theta \in [-r,0]$, it follows from the first of Eq. (7.3) that

$$\lim_{t\to 0+} t^{-1}[T(t)\phi(\theta) - \phi(\theta)]$$

exists only at points where the right-hand derivative $\phi'(\theta+)$ exists, and its value is $\phi'(\theta+)$. If $\theta=0$, the second equation in (7.3) yields

$$\lim_{t\to 0+} t^{-1}[T(t)\phi(0) - \phi(0)] = \lim_{t\to 0+} t^{-1} \int_{0}^{t} L(T(s)\phi)ds = L(T(0)\phi) = L(\phi).$$

It follows that $\phi \in D(A)$ if and only if ϕ has a right-hand derivative on [-r,0), ϕ' , which with the value $L(\phi)$ at $\theta=0$ comprise a function in C. This result is summarized in the next lemma.

Lemma 7.2. The infinitesimal generator A of $\{T(t), t \ge 0\}$ has domain $D(A) = \{\phi \in C: \phi \text{ has a continuous derivative on } [-r,0] \text{ and } \phi(0) = L(\phi)\}.$ For $\phi \in D(A)$,

$$(A\phi)(\theta) = \begin{cases} \phi'(\theta), & -r \leq \theta < 0 \\ L(\phi) = \phi'(0), & \theta = 0 \end{cases}$$

D(A) is dense in C and Eq. (7.5) holds for $\phi \in D(A)$.

Briefly, we may say that $A\phi = \phi$. We shall now compute the spectrum and resolvent operator of A. Consider the equation

$$(7.8) (A-\lambda I)\phi = \psi$$

where $\psi \in C$, $\phi \in D(A)$. This is $\phi'(\theta) - \lambda \phi(\theta) = \psi(\theta)$, $\theta \in [-r, 0]$. This has solutions

(7.9)
$$\phi(\theta) = e^{\lambda \theta}b + \int_0^{\theta} e^{\lambda(\theta - u)} \psi(u) du, \quad \theta \in [-r, 0]$$

where b is a constant vector. ϕ will be in D(A) if $\phi'(0) = L(\phi)$, that is,

$$\lambda b + \psi(0) = \int_{-r}^{0} [d\eta(\theta)] \{e^{\lambda \theta}b + \int_{0}^{\theta} e^{\lambda(\theta - \mathbf{u})} \psi(\mathbf{u}) d\mathbf{u}\}.$$

This simplifies to

(7.10)
$$\Delta(\lambda)b = -\psi(0) + \int_{-r}^{0} \int_{0}^{\theta} e^{\lambda(\theta - \mathbf{u})} d\eta(\theta)\psi(\mathbf{u})d\mathbf{u}$$
(7.11)
$$\Delta(\lambda) = \lambda \mathbf{I} - \int_{0}^{0} e^{\lambda\theta} d\eta(\theta).$$

Since the right member of (7.10) can assume any value in \mathbb{R}^n , by choice of $\psi \in \mathbb{C}$, it follows that Eq. (7.8) is solvable for b for every $\psi \in \mathbb{C}$ if and only if $\det \Delta(\lambda) \neq 0$. If $\det \Delta(\lambda) \neq 0$, there is a unique solution $\phi \in D(A)$ given by Eq. (7.9). Thus, Eq. (7.9) shows that the inverse $(A-\lambda I)^{-1}$ exists if $\det \Delta(\lambda) \neq 0$, with domain of all \mathbb{C} , and $(A-\lambda I)^{-1}$ is a bounded linear map since the map $\psi \mapsto b$ is bounded and so is the map from (b,ψ) to ϕ given by (7.9). Consequently, if $\det \Delta(\lambda) \neq 0$, then λ is in the resolvent set of A. On the other hand, if $\det \Delta(\lambda) = 0$, then there exists b for which $\Delta(\lambda)b = 0$ and if we let $\phi(\theta) = e^{\lambda \theta}b$ then $\Delta(\theta) = \lambda e^{\lambda \theta}b$, so $\Delta(0) = \lambda \phi$ and λ is an eigenvalue with eigenfunction ϕ . This result may be summarized as follows.

<u>Lemma 7.3.</u> The spectrum of A consists entirely of point spectrum, $P\sigma(A)$, that is points in the sp(A) are eigenvalues, and

$$P\sigma(A) = \{\lambda \in \mathbb{C}: det \Delta(\lambda) = 0\}.$$

If λ is in the resolvent set of A, then $(A-\lambda I)^{-1}$ is defined by $(A-\lambda I)^{-1}\psi=\phi$ where ϕ is given by Eq. (7.9) and (7.10).

The equation $\det \Delta(\lambda) = 0$ is called the <u>characteristic equation</u> and its roots are called the <u>characteristic roots</u>. The following properties of the eigenvalues λ_4 of A are known (see Hale, (1977), Bellman and Cooke (1963)).

- (i) Each λ_i is of finite multiplicity.
- (ii) All eigenvalues lie in some left half plane $\text{Re}\lambda \leq \text{constant.}$
- (iii) When η is piecewise constant, as it is for a differential difference equation, the λ_j of large modulus lie in curvilinear strips of type |Re(s+μlog s)| ≤ constant.

In Chapter 3 we shall say more about conditions under which all $\operatorname{Re}\lambda_{j} < 0$. We now state a number of additional properties, without proof because of lack of space. Let λ be an eigenvalue of A and let $\operatorname{M}_{\lambda}$ denote the smallest subspace of C containing all the null spaces $\operatorname{N}(A-\lambda I)^{p}$, $\operatorname{p=1,2,...}$ Since $\det \Delta(\lambda)$ is an entire function of λ , it has zeros of finite order. So the resolvent function $(\lambda I-A)^{-1}$ has only poles of finite order. This together with the fact that A is a closed operator imply that $\operatorname{M}_{\lambda}$ is finite dimensional and for some integer k,

$$M_{\lambda} = N(A-\lambda I)^{k}$$
.

Also, k is the algebraic multiplicity of λ , and moreover the dimension of M_{λ} is k (Levinger (1968)). M_{λ} is called the <u>generalized eigenspace</u> of λ_{i} . The following additional properties are known:

Theorem 7.1

(i)
$$C = N(A-\lambda I)^k + R(A-\lambda I)^k$$

that is, C is the direct sum of the null space and range of $\left(A-\lambda I\right)^k$.

(ii)
$$AM_{\lambda} \subseteq M_{\lambda}$$
 and $T(t)M_{\lambda} \subseteq M_{\lambda}$.

(iii) Let d be the dimension of M_{λ} and let ϕ^1,\ldots,ϕ^d be a basis for M_{λ} . Let Φ_{λ} denote the $n\times d$ matrix-valued function, $\Phi_{\lambda}\colon [-r,0]\to \mathbb{R}^{nd}$,

(7.12)
$$\phi_{\lambda}(\theta) = [\phi^{1}(\theta), \dots, \phi^{d}(\theta)], \quad \theta \in [-r, 0]$$

Then there is a constant $d \times d$ matrix B such that

$$(7.13) A\Phi_{\lambda} = \Phi_{\lambda}B.$$

Moreover, the spectrum of B is the single point $\{\lambda\}$, and

(7.14)
$$\Phi_{\lambda}(\theta) = \Phi_{\lambda}(0)e^{B\theta}, \quad \theta \in [-r, 0].$$

<u>Proof.</u> For most of the proof we refer to Hale (1977), but we make the following observations. Since M_{λ} is invariant under A and Φ_{λ} spans M_{λ} , each column of $A\Phi_{\lambda}$ is a linear combination of elements of Φ_{λ} , hence (7.13) must hold for some matrix B. To get the expression (7.14), note that each element of Φ_{λ} is in the domain of A. Hence by (7.13)

$$\frac{d}{dt} T(t) \phi_{\lambda} = T(t) A \phi_{\lambda} = T(t) \phi_{\lambda} B.$$

Since the semigroup is strongly continuous, this implies that $T(t)\phi_{\lambda} = \phi_{\lambda}e^{Bt}$. Now since each column of $T(t)\phi_{\lambda}$ is a solution of RFDE, and not just the evolution equation, there exists a matrix $W:[-r,\infty)\to\mathbb{R}^{nd}$ such that

$$(\mathtt{T}(\mathtt{t})\,\varphi_{\lambda})\,(\theta)\,=\,\mathtt{W}(\mathtt{t}+\theta)\,,\qquad \mathtt{t}\,\geq\,0\,,\qquad \theta\,\in\,[-\mathtt{r}\,,0\,]\,.$$

This is also $(T(t+\theta)\phi_{\lambda})(0)$ if $t+\theta \ge 0$. Therefore, since $T(t)\phi_{\lambda} = \phi_{\lambda}e^{Bt}$,

we get

$$(\mathtt{T}(\mathsf{t} + \theta) \, \boldsymbol{\varphi}_{\lambda}) \, (0) \, = \, \boldsymbol{\varphi}_{\lambda} \, (0) \, e^{\mathsf{B} \, (\mathsf{t} + \theta)} \, = \, \boldsymbol{\varphi}_{\lambda} \, (\theta) \, e^{\mathsf{B} \, \mathsf{t}} \, , \quad \mathsf{t} \, + \, \theta \geq 0 \, .$$

Taking $t \ge r$ gives

$$\Phi_{\lambda}(\theta) = \Phi_{\lambda}(0)e^{B\theta}, \quad \theta \in [-r, 0].$$

This proves (7.14).

Also note that the relation

(7.15)
$$(T(t)\phi_{\lambda})(\theta) = \phi_{\lambda}(0)e^{B(t+\theta)}, \quad \theta \ge [-r,0]$$

permits us to define T(t) on M_{λ} for all $t \in (-\infty, \infty)$, not just $t \ge 0$. The significance of this is that on a generalized eigenspace of an eigenvalue λ of A, the RFDE has the same structure as an ordinary differential equation. The total contribution of all other eigenvalues does not affect the behavior on the particular generalized eigenspace. The Jordan block structure of B has been described by Kappel (1976b).

By introducing an adjoint operator A*, we can more explicitly characterize $R(A-\lambda I)^k$ in the decomposition of C. Let \mathbb{R}^{n^*} be the n-dimensional Euclidean space of row vectors. For $\phi \in C([-r,0],\mathbb{R}^n)$ and $\psi \in C([\theta,r],\mathbb{R}^{n^*})$ define the bilinear functional that takes the pair (ϕ,ψ) into the number

$$(7.16) \qquad \langle \psi, \phi \rangle = \psi(0)\phi(0) - \int_{-r}^{0} \int_{0}^{\theta} \psi(u-\theta) d\eta(\theta)\phi(u) du .$$

This functional is not necessarily non-degenerate. Also, define an operator \mathbf{A}^{\star} by

(7.17)
$$(A*\psi)(\theta) = \begin{cases} -\frac{d\psi(\theta)}{d\theta}, & 0 < \theta \le r \\ \int_{-r}^{0} \psi(-s)d\eta(s), & \theta = 0 \end{cases}$$

where $D(A^*) = \{ \psi \in C([0,r], \mathbb{R}^{n^*}) : \psi \text{ has a continuous derivative on } [0,r]$ and the derivative at $\theta = 0$ is as specified in (7.17).}

The operator A* is called the <u>formal adjoint</u> of A relative to the bilinear form (7.16), and it is known that it has properties similar to a true adjoint. In particular

$$\langle \psi, A \phi \rangle = \langle A * \psi, \phi \rangle$$
 for all $\phi \in D(A), \psi \in D(A*)$.

A number λ is in the spectrum of A if and only if λ is in the spectrum of A*. Let Ψ_{λ} denote the matrix analogous to Φ_{λ} , that is, let $\Psi_{\lambda} = \operatorname{col}(\psi^1, \dots, \psi^d)$ be a basis for $M_{\lambda}(A^*)$, the generalized eigenspace of λ for A*. Let $\langle \Psi_{\lambda}, \Phi_{\lambda} \rangle$ denote the numerical d by d matrix with ij the element $\langle \psi^i, \phi^j \rangle$. Then $\langle \Psi_{\lambda}, \Phi_{\lambda} \rangle$ is nonsingular and the matrices $\Psi_{\lambda}, \Phi_{\lambda}$ may be chosen so that $\langle \Psi_{\lambda}, \Phi_{\lambda} \rangle = I$. Also we have a version of the Fredholm alternative:

Lemma 7.4. A necessary and sufficient condition for

$$(A-\lambda I)^k \phi = \psi \qquad (\psi \in C)$$

to have a solution ϕ , where k is an integer, is that $\langle \alpha, \psi \rangle = 0$ for all α in the null space of $(A^*-\lambda I)^k$. (Loosely: ψ is in the range of $(A-\lambda I)^k$ if and only if it is "orthogonal" to all α in the null space of $(A^*-\lambda I)^k$.)

Lemma 7.5. Let λ be in the spectrum of A and let

$$\begin{split} & P_{\lambda} = M_{\lambda}(A) = \{\phi \in C | \phi = \Phi_{\lambda}b \text{ for some vector } b \} \\ & Q_{\lambda} = \{\phi \in C | \langle \Psi_{\lambda}, \phi \rangle = 0\} = R(A - \lambda I)^{k}. \end{split}$$

Then the decomposition of C is given explicitly by

$$C = P_{\lambda} \oplus Q_{\lambda}$$