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DELAY DIFFERENTIAL OPERATORS AND SOME SOLVABLE MODELS IN LIFE SCIENCES

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Abstract. Using the methods of the spectral theory of differential operators in Hilbert spaces L^2-solvability of some models arising in mathematical biology are investigated. Particularly, concrete solvable models are given.

1. Introduction

It is known that the general theory of extension of densely defined linear operators in Hilbert spaces was initiated by J. von Neumann in his seminal work [17] in 1929 (for more detail analysis see [18]). Later in 1949 and 1952 M.I. Vishik [22,23] has studied the boundedly (compact, regular and normal) invertible extensions of any unbounded linear densely defined operator in Hilbert spaces. The generalization of these results to the nonlinear and completely additive Hausdorff topological spaces have been done by B.K. Kokebaev, M. Otelbaev and A.N. Synybekov [for example, see 16].

Another approach to the description of regular extensions for some classes of linear differential operators in Hilbert spaces of vector-functions on finite intervals has been offered by A.A. Dezin [3].

It is known that many problems arising in life sciences for example in electrodynamics, control theory, ecology, economy, chemistry, medicine, epidemiology, tumor growth, neutral networks, biology and etc. can be expressed as boundary or initial value problems the linear functional (time proportional or time delay) differential equations in the corresponding functional spaces (for detailed analysis see [1,2,4,5,6,19,20]).

The main goal in all these theories is to obtain clear expressions of exact solutions of the considered problems. Note that all these problems are strongly connected to the with solvability of initial or boundary value problems for considered differential equations in corresponding functional spaces (for special cases see [7-14,24]).

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Problems in this area have not been investigated successfully. Of course, there are approximative and numerical results in these investigations.

Let us remember that an operator $A : D(A) \subset H \to H$ in a Hilbert space H is called boundedly solvable, if A is one-to-one, $AD(A) = H$ and $A^{-1} \in L(H)$. The theory of boundedly solvable extensions of a linear densely defined closed operator in Hilbert or Banach spaces has been investigated by M. I. Vishik [22,23], M. O. Otelbayev (with his scientific group) [16], A. A. Dezin [3] and etc.

From the mathematical literature it is known that the general solution of differential–operator equation

$$u'(t) + A(t)u(t-\tau) = 0,\ \tau > 0$$

with continuous on uniformly operator topology coefficient at finite interval can be represented via evolution operators. Unfortunately, in the infinite interval case since the structure of spectrum $\sigma(A \otimes S_\tau)$ of the operator $A \otimes S_\tau \in L\left(H \otimes L^2(J)\right)$ (H is a Hilbert space, $J \subset \mathbb{R}$ infinite interval $S_\tau u(t) = u(t-\tau),\ (A \otimes S_\tau)\, u(t) = A(t)u(t-\tau)]$) is not clear, then general solution of above retarded type delay differential equation can not be written via evolution operators in corresponding L^2- spaces. This creates many theoretical difficulties. Note that investigation of these problems in special cases by difference scheme method is reduced to the study of spectral properties of infinite upper or lower triangular double-banded matrices over corresponding sequence spaces (for example, see [15] and references therein). In this work to overcome this obstacle so-called many-Hilbert space-method is applied.

In this paper before all of these, in section 2, using the many-Hilbert space-method all L^2-boundedly solvable extensions of the minimal operator generated by multipoint differential-operator expression for first order in the Hilbert space of vector-functions are described. Lastly, in section 3, the obtained results to concrete mathematical models arising in life sciences are applied.

2. Boundedly Solvable Extensions

Throughout this work (a_n) is a real number sequence with properties $a_0 < a_1 \leq a_2 < a_3 \leq ... \leq a_{n-1} < a_n < ...,\ \lim\limits_{n\to+\infty} a_n = +\infty,\ H_n$ is a separable Hilbert space, $J_n = (a_{n-1}, a_n),\ \mathcal{H}_n = L^2(H_n, Jn),\ n \geq 1$ and $\mathcal{H} = \bigoplus\limits_{n=1}^{\infty} \mathcal{H}_n$.

We consider the following linear multipoint differential-operator expression of first order in $\mathcal{H}$ in form

$$l(u) = (l_n(u_n)),\ u = (u_n),$$

where

(1): $l_1(u_1) = u_1'(t) + A_1(t)u_1(t)$ and $l_n(u_n) = u_n'(t) + A_n(t)u_n(t) + B_{n-1}(t)u_{n-1}(t)$, $n \geq 2$;

(2): operator-function $A_n(\,\cdot\,) : [a_{n-1}, a_n] \to L(H_n)$, $B_n(\,\cdot\,) : [a_{n-1}, a_n] \to L(H_n)$, $n \geq 1$ is continuous on the uniformly operator topology and $\sup\limits_{n\geq 1}\sup\limits_{t\in J_n} |J| \|A_n(t)\| < \infty$.

Actually, the differential expression $l(\,\cdot\,)$ in $\mathcal{H}$ can be written in following form

$$l(u) = u'(t) + A(t)u(t) + B(t)u(t), \tag{2.1}$$

where: $u = (u_n)$ and for $t > a_0$

$$A(t) = \begin{pmatrix} A_1(t) & & & & \\ & A_2(t) & & 0 & \\ & & \ddots & & \\ & 0 & & A_n(t) & \\ & & & & \ddots \end{pmatrix},$$

$$B(t) = \begin{pmatrix} 0 & & & & & \\ B_1(t) & 0 & & 0 & & \\ & B_2(t) & 0 & & & \\ & & \ddots & \ddots & & \\ & 0 & & B_{n-1}(t) & 0 & \\ & & & & \ddots & \ddots \end{pmatrix}$$

The operators $L_0(M_0)$ and $L(M)$ are minimal and maximal operators corresponding to $l(\,\cdot\,)$(and $m(\,\cdot\,) = \frac{d}{dt} + A(\,\cdot\,)$) in $\mathcal{H}$, respectively. It is clear that

$$L_0 = M_0 + B(\,\cdot\,),\ L = M + B(\,\cdot\,).$$

On the other hand for each $n \geq 1$ by standard way the minimal operator M_{n0} and maximal operator M_n corresponding to the differential expression $m_n(\,\cdot\,) = \frac{d}{dt} + A_n(\,\cdot\,)$ in $\mathcal{H}_n$ can be defined. It is clear that $D(M_{n0}) = \overset{o}{W}{}_2^1(H_n, J_n)$ and $D(M_n) = W_2^1(H_n, J_n)$, $n \geq 1$.

Firstly, the main purpose in this section is to describe all boundedly solvable extensions of the minimal operator M_0 in $\mathcal{H}$ in terms of boundary values. We first give some results from work [10].

Theorem 2.1. If $\widetilde{M}$ is any extension of M_0 in $\mathcal{H}$, then $\widetilde{M} = \bigoplus\limits_{n=1}^{\infty} \widetilde{M}_n$, where $\widetilde{M}_n$ is a extension of M_{n0} in $\mathcal{H}_n$, $n \geq 1$.

Theorem 2.2. For the boundedly solvability of any extension $\widetilde{M} = \bigoplus\limits_{n=1}^{\infty} \widetilde{M}_n$ of the minimal operator M_0 in $\mathcal{H}$, the necessary and sufficient conditions are the boundedly solvability of the coordinate extensions $\widetilde{M}_n$ of the minimal operators M_{n0} in $\mathcal{H}_n$, $n \geq 1$ and $\sup\limits_{n\geq 1} \|\widetilde{M}_n^{-1}\| < \infty$.

Theorem 2.3. Let $n \geq 1$. Each boundedly solvable extension $\widetilde{M}_n$ of the minimal operator M_{n0} in $\mathcal{H}_n,\ n \geq 1$ is generated by the differential-operator expression $m_n(\,\cdot\,)$ and the boundary condition

$$(K_n + E_n)u_n(a_{n-1}) = K_n exp\left(-\int\limits_{J_n} A_n(s)ds\right)u_n(a_n), \tag{2.2}$$

where $K_n \in L(H_n)$ and $E_n : H_n \to H_n$ is an identity operator. The operator K_n is determined by the extension $\widetilde{M}_n$ uniquely, i.e. $\widetilde{M}_n = M_{K_n}$.

On the contrary, the restriction of the maximal operator M_n in $\mathcal{H}_n$ to the linear manifold of vector-functions satisfying the condition (2.2) for some bounded operator $K_n \in L(H_n)$ is a boundedly solvable extension of the minimal operator M_{n0}.

On the other hand for each $n \geq 1$

$$\|\widetilde{M}_{K_n}^{-1}\| \leq 2|J_n|\,(1 + \|K_n\|)\, exp\left(2|J_n| \sup_{t \in J_n} \|A_n(t)\|\right)$$

Theorem 2.4. Let us assumed that $\sup\limits_{n\geq 1} |J_n| \|K_n\| < \infty$. Each boundedly solvable extension $\widetilde{M}$ of the minimal operator M_0 in $\mathcal{H}$ is generated by differential-operator expression $m(\,\cdot\,)$ and the boundary conditions

$$(K_n + E_n)u_n(a_{n-1}) = K_n exp\left(-\int\limits_{J_n} A_n(s)ds\right)u_n(a_n), \quad n \geq 1$$

where $K_n \in L(H_n)$, $K = \bigoplus\limits_{n=1}^{\infty} K_n \in L\left(\bigoplus\limits_{n=1}^{\infty} H_n\right)$ and $E_n : H_n \to H_n$ is an identity operator, $n \geq 1$. The operator K is determined by the extension $\widetilde{M}$ uniquely, i.e. $\widetilde{M} = M_K$ and vice versa.

Theorem 2.5. If $K = \bigoplus\limits_{n=1}^{\infty} K_n \in L\left(\bigoplus\limits_{n=1}^{\infty} H_n\right)$ and $M_K = \bigoplus\limits_{n=1}^{\infty} M_{K_n}$ is a boundedly solvable extension of the minimal operator M_0 and satisfies the following condition $\|M_K^{-1}B(\,\cdot\,)\| = \sup\limits_{n\geq 1} \|M_{K_{n+1}}^{-1}B_n(\,\cdot\,)\| < 1$, then the operator $L_K = M_K + B(\,\cdot\,)$ is boundedly solvable in $\mathcal{H}$.

3. Application in Life Sciences

Example 3.1 [19]. Consider the following linearized logistic delay differential equation (or Hutchinson's model)

$$\dot{x}(t) = rx(t - \tau),\ \tau > 0,\ t > 0$$

with history function $x(t) = \varphi(t),\ -\tau \leq t \leq 0$, where $\varphi \in C[-\tau, 0]$.

This problem can be written in form

$$\begin{cases} \dot{x}_1(t) = r\varphi(t-\tau),\ 0 < t < \tau, \\ \dot{x}_n(t) = rx_{n-1}(t),\ (n-1)\tau < t < n\tau,\ n \geq 2. \end{cases} \tag{3.1}$$

By Theorem 2.3. all boundedly solvable extension M_{K_n} of the minimal operator M_{n0} in $\mathcal{H}_n = L^2((n-1)\tau, n\tau)$ is generated by the differential expression $m_n(x) = x_n'(t)$ and boundary condition

$$(k_n+1)x_n((n-1)\tau) = k_n x_n(n\tau),\ k_n \in \mathbb{C},\ n \geq 1$$

and vice versa. On the other hand in this case for $\sup\limits_{n\geq 1}|k_n| < \infty$ we have

$$\sup_{n\geq 1}|J_n|\,(1+|k_n|) = \tau\left(1+\sup_{n\geq 1}|k_n|\right) < \infty.$$

Then by Theorem 2.4. the extension $\bigoplus\limits_{n=1}^{\infty} M_{K_n}$ in $L^2(0,\infty)$ is boundedly solvable. Moreover, the following inequality

$$\begin{aligned} \sup_{n\geq 1}\|M_{k_{n+1}}^{-1}B_n(\,\cdot\,)\| &\leq \sup_{n\geq 1}\|M_{k_{n+1}}^{-1}\|\|B_n(t)\| \\ &= \sup_{n\geq 1}\sqrt{2}\tau\,(1+|k_n|)\,|r|\sqrt{\tau} = \sqrt{2}\tau^{3/2}|r|\left(1+\sup_{n\geq 1}|k_n|\right) \end{aligned}$$

implies that if $\sqrt{2}\tau^{3/2}|r|\left(1+\sup\limits_{n\geq 1}|k_n|\right) < 1$, then by Theorem 2.5. the following equation (3.1) has a solution in the form

$$x_1(t) = rk_1\int_0^{\tau}\varphi(t-s)ds + r\int_0^{t}\varphi(\tau-s)ds,\ 0 < t < \tau,$$

$$x_n(t) = rk_n\int_{(n-1)\tau}^{n\tau} x_{n-1}(s)ds + r\int_{(n-1)\tau}^{t} x_{n-1}(s)ds,\ (n-1)\tau < t < n\tau,\ n \geq 2.$$

Example 3.2 [19]. Consider the following linearized Houseflies Model (Musca domestica) in form

$$\dot{x}(t) = -dx(t) + bx(t-\tau),\ t > 0,$$

where: $x(\,\cdot\,)$ is the number of adults, $d > 0$ denotes the death rate of adults, the time delay $\tau > 0$ is the length of the developmental period between oviposition and eslosion of adults, $b > 0$ is the number of eggs laid by pair adults, with history function

$$x(t) = \psi(t),\ -\tau \leq t \leq 0,\ \psi \in C[-\tau, 0].$$

This problem (that is, description of oscillations of the adults' numbers in laboratory populations) can be written in following form

$$\begin{cases} \dot{x}_1(t) = -dx_1(t) + b\psi(t-\tau),\ 0 < t < \tau, \\ \dot{x}_n(t) = -dx_n(t) + bx_{n-1}(t),\ (n-1)\tau < t < n\tau,\ n \geq 2 \end{cases}$$

in the direct sum of Hilbert spaces $\mathcal{H} = \bigoplus_{n=1}^{\infty} L^2\left((n-1)\tau, n\tau\right)$. Again by Theorem 2.3. all solvable extensions M_{K_n} of the minimal operator M_{n0} in $\mathcal{H}_n = L^2\left((n-1)\tau, n\tau\right)$ is generated by the differential expression $m_n(x_n) = \dot{x}_n(t) + dx_n(t)$ and boundary condition $(k_n+1)x_n\left((n-1)\tau\right) = k_n exp(-d\tau)x_n(n\tau),\ k_n \in \mathbb{C},\ n \geq 1$ and vice versa.

If $\sup_{n\geq 1}|k_n| < \infty$, then by Theorem 2.4. the extension $\bigoplus_{n=1}^{\infty} M_{k_n}$ in $L^2(0,\infty)$ is boundedly solvable. Moreover, from the following computations

$$\sup_{n\geq 1}\|M^{-1}_{k_{n+1}}(-b)\| \leq \sup_{n\geq 1}\left[2\tau\left(1+|k_n|\right)exp(2\tau d)b\right]$$

implies that if

$$\tau b\left(1+\sup_{n\geq 1}|k_n|\right)exp(2\tau d) < \frac{1}{2},$$

then by Theorem 2.5. the considered problem has a L^2-solution.

Example 3.3 [21]. Consider the following delay case Drug-free model in the absence of immune response

$$T_I'(t) = 2a_4 T_M(t) - d_2 T_I(t) - a_1 T_I(t-\tau),$$

$$T_M'(t) = a_1 T_I(t-\tau) - dT_M(t),\ \tau > 0,\ t > 0$$

with history functions

$$T_I(t) = \psi_0(t),\ t \in [-\tau, 0],\ T_M(t) = \psi_1(t),\ t \in [-\tau, 0].$$

Here $T_I(t)$ is a population of tumor cells during interphase at time $t > 0,\ T_M(t)$ is a tumor population during mitosis at time $t > 0,\ T > 0$ is a resident time of cells in interphase, a_1 and a_4 represent the different rates at which cells cycle or reproduce, $d_2 T_I$ and $d_3 T_M$ represent propositions of natural cell death or apoptosis, $d = d_3 + a_4$.

To solve this system of delay differential equations with mentioned history functions consider the following matrix form

$$T'(t) = AT(t) + BT(t-\tau),\quad \tau > 0,\ t > 0$$

where: $T(t) = \left(T_I(t), T_I(t)\right)^T$,

$$A = \begin{pmatrix} -d_2 & 2a_4 \\ 0 & -d \\ & \end{pmatrix},\ \ \mathbb{R}^2 \to \mathbb{R}^2 \text{ and } B = \begin{pmatrix} -a_1 & 0 \\ a_1 & 0 \\ & \end{pmatrix},\ \ \mathbb{R}^2 \to \mathbb{R}^2$$

in the direct sum of Hilbert spaces $L^2\left(\mathbb{R}^2,(0,\infty)\right)=\bigoplus_{n=1}^{\infty} L^2\left(\mathbb{R}^2,((n-1)\tau,n\tau)\right)$.

By Theorem 2.3 all solvable extensions M_{k_n} of the minimal operator M_{n0} in $\mathcal{H}_n=L^2\left(\mathbb{R}^2,((n-1)\tau,n\tau)\right)$ are generated by the differential expression

$$m_n(T_n)=\dot{T}_n(t)+(-A)T_n(t),\ n\geq 1$$

and boundary condition $(k_n+1)T_n((n-1)\tau)=k_n exp(A\tau)T_n(n\tau),\ k_n\in\mathbb{R}^2,\ n\geq 1$ and vice versa.

In case when $\sup\limits_{n\geq 1}|k_n|<\infty$, we have $\tau\left(1+|k_n|\right)exp(2\tau\|A\|)<\infty$. Consequently, by Theorem 2.4. the extension $\bigoplus_{n=1}^{\infty} M_{k_n}$ is boundedly solvable in $L^2\left(\mathbb{R}^2,(0,\infty)\right)$.

On the other hand it is clear that if

$$\sup_{n\geq 1}\|M_{k_n}^{-1}B\|\leq\sup_{n\geq 1}2\tau\left(1+|k_n|\right)exp(2\tau\|A\|)\|B\|<1,$$

then by Theorem 2.5. above considered problem has a unique L^2-solution.

Example 3.4 [19]. Consider the following special multiple delay logistic model in the linear case

$$\dot{x}(t)=ax(t-\tau)+bx(t-2\tau),\ \tau>0,\ t>0,\ a,b\in\mathbb{R}$$

in $L^2(0,\infty)$ with history function $\dot{x}(t)=\psi(t),\ -2\tau<t<0$. These problems with two delays appear in neurological models, physiological models, medical models, epidemiological models and etc.

This problem can be written in $L^2(0,\infty)=\bigoplus_{n=1}^{\infty} L^2\left((n-1)\tau,n\tau\right)$ in following form

$$l(x)=\begin{cases} x_1'(t)+a\psi(t-\tau)+b\psi(t-2\tau),\ 0<t<\tau,\\ x_n'(t)+ax_{n-1}(t)+bx_{n-2}(t),\ (n-1)\tau<t<n\tau,\ n\geq 2\end{cases}$$

Again by Theorem 2.3 all solvable extensions M_{k_n} of the minimal operator M_{n0} in $\mathcal{H}_n=L^2((n-1)\tau,n\tau)$ are generated by the differential expression $m_n(x_n)=\dot{x}_n(t)$ and boundary condition $(k_n+1)x_n((n-1)\tau)=k_n x_n(n\tau),\ k_n\in\mathbb{C},\ n\geq 1$ and vice versa.

If $\sup\limits_{n\geq 1}|k_n|<\infty$, then by Theorem 2.4 the extension $M=\bigoplus_{n=1}^{\infty} M_{K_n}$ is boundedly solvable in $L^2(0,\infty)$. In addition, if

$$\|M_k^{-1}C\|\leq\sqrt{2}\tau\left(1+\sup_{n\geq 1}\|k_n\|\right)\left(2|b|^2+3|a|^2\right)<1,$$

then by Theorem 2.5. the considered above problem has a L^2-solution.

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