Integral-Spectral Methods Applied to Healthcare Engineering: A Student-Focused Pedagogical Approach

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Abstract

The human body has numerous biophysical systems to support life that contain many variables such as temperature, concentration of nutrients, oxygen, carbon dioxide and many others. These variables are mathematically present in both linear and non-linear processes that are needed to maintain healthy conditions in the body and, more frequently than not, to assist in its healing. There is a great pedagogical need and also a high mathematical challenge to handle these processes in an efficient way. Integral-Spectral Methods (ISM) allows for the handling of these terms by decoupling the linear aspects (i.e. transport-based terms) and the non-linear aspects (i.e. kinetics/generation-based terms). However, becoming familiar with ISM usually shows learning challenges for the students due to the lack of a systematic and pedagogical introduction to the subject in textbooks. This paper aims to outline a systematic and well-organized approach to learn ISM without the mathematical difficulty presently found in textbooks. Once a proper approach is established, examples in healthcare engineering to which ISM may be applied is presented, with one example being a cancerous tumor undergoing drug treatment. This example illustrates well the linear and nonlinear aspects previously mentioned, and the simulation of this treatment is a very important step in assessing treatment in cancer tumors. This approach also allows for a certain "flexibility" through which the "healing function" can be manipulated. This is essential in properly planning customized treatments for patients undergoing drug or other treatments. Details about the different aspects needed in the creation of a friendly pedagogical approach to ISM will be summarized.

Keywords

Integral-Spectral Methods, engineering modeling, healthcare engineering, mathematical oncology

Introduction

Cancerous tumors often consist of very complex systems with multiple domains and multiple phenomena occurring simultaneously within each domain.[1]These complexities motivate the need for a description of a potential treatment with greater mathematical sophistication. Integral-Spectral Methods (ISM) is the ideal approach for solving engineering problems in healthcare, such as the treatment of cancerous tumors, because it provides a flexibility not found in other mathematical approaches. ISM is a systemization composed of two key components: operator-theoretic methods (in place of matrix-based approaches) and integral equations.[2] The combination of these two components allows for a methodical description of the health care problem which is applicable to a variety of other situations. Some examples of problems that can be tackled using ISM include hyperthermia treatment of cancerous tumors, drug delivery, and hemodialysis, etc. where each of these healthcare treatments each have their own levels of complexity.

Pedagogical Framework

A. General Overview:

In order to apply the ISM approach to solve these problems, one will find it useful to follow the *ISM Implementation Cycle* which can be seen in Figure 1. The role of this cycle is to serve as a roadmap to the learner/modeler, and to provide a step-by-step approach to solving the problem. In order to begin the *ISM Implementation Cycle*, a healthcare problem and its desired solution must be identified. Once the problem is identified, the operator-based differential problem (DOP) is formulated. Then, using a Green's function approach, the DOP can be inverted and the integral equation obtained. Upon identification of the Green's function, the problem can be solved and results illustrated. These results (rate of cell killing, temperature profiles, etc.) can then be communicated to medical doctors in order to help guide them to adjust parameters in order to achieve a more effective treatment to patients. A major goal of this work is to present an approach in which the engineer may develop a model for a specific healthcare treatment. Medical doctors may then input patient-specific parameters (either physical values related to diffusion or drug reaction rates, etc.) into the model and predict ranges of effectiveness of a treatment based on a customized/optimized treatment.

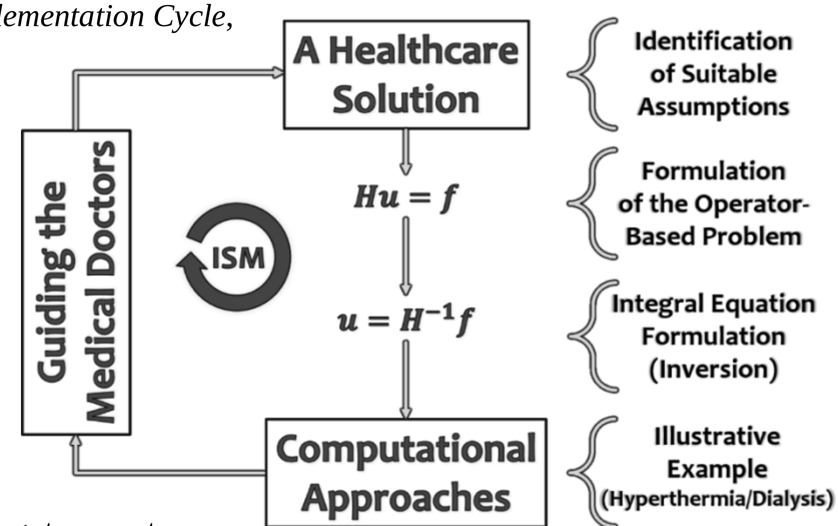

Figure 1. ISM Implementation Cycle

B. Connections with the Fundamentals:

In order to illustrate the connection between the mathematic fundamentals and the healthcare application, we will present a general convective-diffusive case (transport in the artery) where the non-dimensional form of the transport equation is represented as

$$\alpha r(1-r^2)\frac{\partial C}{\partial z} = \frac{\partial}{\partial r}\left(r\frac{\partial C}{\partial r}\right) + rF(C) \quad (1)$$

From equation (1), the higher-order differential term is connected with the diffusion of the drug along the radial direction. This is an excellent suggestion to identify the second-order differential operator with the accompanying Hilbert space H associated with the problem as[2]

$$\underset{\approx}{L} = \{L,\ D(L)\} \text{ where, } \quad \begin{matrix} L = -\frac{d}{dr}\left(r\frac{\partial}{\partial r}(\cdot)\right) \\ D(L) = \{w \in H; Lw \in H; w_r(0) = 0; w_r(1) = 0\} \end{matrix} \quad (2)$$

Further, the composite convective-diffusive differential operator is written as follows

$$H_z(\cdot) = \left[\alpha\frac{\partial}{\partial z}(\cdot) + \frac{L(\cdot)}{R(r)}\right] \quad (3)$$

The sources of knowledge for this formulation are from courses 1, 2, 3, and 5 listed in Table 1. From the concept that integral equations are the mathematical inverse of differential equations and by using the Green's function as the kernel[3] we can write the inverse operator H_z^{-1} formulation for the operator H_z as follows

$$C = H_z^{-1}[Q(C)] \tag{4}$$

And, subsequently, the integral inversion of the differential operator problem can be shown

$$\int_0^{z+\varepsilon} dz' \langle G(\underset{\sim}{x}|\underset{\sim}{x}'), H_z C\rangle = \int_0^{z+\varepsilon} dz' \langle G(\underset{\sim}{x}|\underset{\sim}{x}'), F(C)\rangle \tag{5}$$

Where $G(\underset{\sim}{x}|\underset{\sim}{x}')$ in equation (5) is given by the following spectral representation[4]

$$G(\underset{\sim}{x}|\underset{\sim}{x}') = \sum_0^{\infty} A_n^{-2}\, exp\left[\left(-\frac{\lambda_n^2}{\alpha}\right)^n (z - z')\right] \phi_n(r)\phi_n(r')\theta(z - z') \tag{6}$$

The source of math knowledge is found in course 4 in Table 1.

Course	Relevant Contents	Typical Textbooks
1. Linear Algebra	Functions, Domains, Ranges, Matrices (rank, determinants, inverse eigenvalue problems), linear systems of equations, bases and solutions, etc.	• Axler, Sheldon J. *Linear algebra done right*. Springer, 2015. • Strang, Gilbert. *Linear algebra and its applications*. Thomson, Brooks/Cole, 2006.
2. Ordinary Differential Equations - BVPs	Fundamental class of ODEs and BVPs with different types of boundary conditions. The S-L theory and the role in the solution of BVP – Fourier series expansions, etc.	• Boyce, William E., and Richard C. DiPrima. *Elementary differential equations and boundary value problems*. Wiley, 2012. • Strang, Gilbert. *Differential equations and linear algebra*. Wellesley-Cambridge Press, 2014.
3. Partial Differential Equations	First order equations, Classification of second order equations, Wave equation, Laplace equation, Parabolic equations, Green's theorem, Introduction to Green's function	• Weinberger, Hans F. *A first course in partial differential equations with complex variables and transform methods*. Dover Publications, 1995. • John, Fritz. *Partial differential equations*. Springer-Verlag, 1982.
4. Integral Equations	Fundamentals of integral equations, classification and examples of integral equations, integral equations and Green's function as kernels, Green's function definition and properties, derivation of Green's function via separation of variables approach and method of images	• Haberman, Richard. *Elementary applied partial differential equations : with Fourier series and boundary value problems*. Prentice Hall, 1998. • Stakgold, Ivar, and Michael J. Holst. *Green's functions and boundary value problems*. Wiley, 2011.
5. Linear Operator Theory and Methods	Fundamentals of linear operator theory, linear spaces: classification and examples, inner products, norms, linear operators: terminology, notation, characteristics, differential operators, self-adjoint operators, Sturm-Liouville problem	• Davis, H T., and Kendall T. Thomson. *Linear algebra and linear operators in engineering : with applications in Mathematica*. Academic Press, 2000. • Ramkrishna, Doraiswami, and Neal R. Amundson. *Linear operator methods in chemical engineering with applications to transport and chemical reaction systems*. Prentice-Hall, 1985 • Naylor, Arch W., and George R. Sell. *Linear operator theory in engineering and science*. Springer, 2000.

Table 1. Relevant Courses for ISM

Once the Green's function is obtained, the modeler can then progress to obtain the solution (along with the appropriate eigenfunctions and eigenvalues) to the model. The inherent flexibility in the solution is a great advantage to the modeler, in that it allows for easy variation of parameters: source/sink functions, etc.

Conclusions and Future Work

In this work, we have outlined a systematic and flexible approach (ISM) that has the ability to describe solutions to healthcare applications. This approach is also progressive in nature in that it can be used to solve a hierarchy of problems in healthcare that consist of different levels of mathematical sophistication. This approach is rooted in advanced mathematical and computational techniques that allows for the description of a range of situations including, for example, hyperthermia, dialysis, kidney malfunction, arterial stenosis among others.[5,6]

References

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