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MATHEMATICS AND BIOLOGY

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ABSTRACT

In India and so many other countries, the science students are generally separated into two main streams: one opting mathematical sciences, the other studying biological sciences. As a result, medicos and biologists have no adequate knowledge of mathematical sciences. It causes a great drawback to them in order to be perfect and updated in their profession, due to the tremendous application of mathematics in bio–sciences, now–a–days. The main aim of this article is to emphasize on the need of the time to produce the mathematico–biologists in abundance for the better service of mankind.

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Mathematics and its applications are now awe-inspiring in their scope, variety and depth. Not only is there rapid growth in pure mathematics and its applications to the traditional fields of the physical sciences, engineering and statistics, but new fields of application have emerged in biology, ecology, geology, genetics, medical sciences and social organizations, etc. The user of mathematics must assimilate subtle new techniques and also learn to handle the great power of the computer efficiently and economically.

Mathematics has proved to be a powerful tool to interact with almost all sciences and it has made a tremendous contribution to ***Physical Sciences*** (physics, chemistry, mechanics, etc.), *Social Sciences* (economics, psychology, sociology, linguistics etc.), *Industrial Sciences* (stock control, allocation, transportation, sequencing, search theory, dynamic programming etc.) *Technological Sciences* (information theory, engineering, network theory, control systems, computers, space technology etc.) and ***Life Sciences*** (genetics, agriculture, medicine, cybernetics etc.). This aspect of mathematics is known as applied mathematics which has a marvellous role in the success and progress of all modern sciences and technologies.

Mathematics entered the field of life sciences through the medium of mathematical statistics because the nature of base structures of life sciences is probabilistic. About three centuries ago, the mathematics was used in the studies of genetic characteristics in peas. Since then the interaction of mathematics gathered momentum in genetics for the improvement in breeds of plants and animals. Pearson used test of significance and sampling distribution for certain applications in biometrics. Fisher did a lot of work at Rothamstead farm for testing the signifiance of the differences between varieties of wheat by using the techniques of analysis of variance and covariance. Moreover, statistical methods, have been playing a drastic role, since long past, in the areas of animal husbandry, industrial quality control, insurance and banking, public health, medicine, psychology and education

The development of cybernetics began during the second world war, after mathematicians Weiner and Bigelow as well as another team composed of McCulloch and Pitts had noticed that machines and organisms show considerable similarity in both structure and function and that both can be described in terms of systems. Considerations on control mechanisms in physiology (the science of functions and phenomena of living beings) first came into the picture in the seventeenth century (Helmont 1660, Descartes 1664) and were published in a more improved and developed form in the 18th century by Seguin and Lavoisier, 1789. The theory of control and regulation arose in the 19th century starting with Borgnis in 1818 and it was further worked out by Maxwell, Farcot and Wischnegradskii. After the discovery of the triode, around the turn of the century, electronic techniques made a rapid developments during the next 50 years. During the second world war, all these fields merged with computer techniques and the theory of automata to become cybernetics, supplemented after the war (1948) by Shannon's communication theory. Cybernetics, in brief, deals with the comparative study of control and communication on the animal and the machine. The mathematical methods and techniques were applied to exploit the analogies between the working of brains and the control computation communication aspects of machines.

The neurophysiological models of the brain are made and their adequacy is tested by mathematico-deductive methods. Though all physiological and psychological problems are not supposed to be solved by application of mathematics, however it is sure that mathematico-deductive methods have taken an important place *besides* the experimental and clinical studies of neurophysiologists and psychologists. The mathematics is helping a biologist in the same way as it helped the electrical engineer to build the electronic computers.

The application of mathematical techniques to biology appeared in the literature in the early twenties. In the thirties and forties and so on, it flourished and now the research papers, journals and magazines on mathematics in medical sciences and biology are plenty in number.

A variety of methods exist for stochastic modelling of infectious diseases. Discrete time stochastic models of epidemic spread based on the chain binomial distribution were first proposed by Reed and Frost in the 1920s.

Markoff chain binomial sampling models of S. Wright (1931) and the ideas given by R.A. Fisher in his book "The Genetical Theory of Natural Selection" (1930) have been widely used in genetic studies of finite populations under the influence of mutation, migration and selection.

A method of measuring principal routes of calcium metabolism in man, given by Aubert and Milhand (1960) is based on comparison of the solution to a certain system of differential equations containing a number of parameters with the observed curve of decreasing radio-activity in the blood.

Around 1964, a mathematical description of the process of inducible enzyme synthesis was presented by Heinmets who set up a complete system of differential equations describing the situation. Later on, in this direction, the techniques of quasilinearization and dynamic programming were developed by R.S. Roth and M.M. Roth from Massachusetts. In 1964, W.W.J. Walton submitted his doctoral dissertation at the John Hopkins University, Baltimore, Maryland, on "Modern Decision Theory Applied to Medical Diagnosis". In 1969, the Medical Institute, Moscow, treated diagnostic process as a control decision stochastic process.

The mathematical research work on the problems of non-Newtonian fluid flow had attracted the attention of biologists due to two mathematical properties of blood flow (I) blood flow in the human body is non-Newtonian fluid with complicated stress-strain rate equation (II) the walls of channels of this blood flow are of varying cross section, curved and elastic. The same feature is also observed in the case of elasticity, fracture and fatique of bones. H.M. Lieberstein (1965) has shown the use of non-linear partial differential equation problems for the velocity in time-dependent flow of a viscous, incompressible fluid in an elastic tube which is intended to represent blood flow in vessels. It is also worthwhile to point out here that the branches of mathematics, namely elasticity and tribology proved very useful tools to biologists in the technical field of movements of human body joints.

The electrophysiological investigations of the physiochemical bases of excitation carried

out by Eccles and Kostynk and many other physiologists laid the foundation for an accurate quantitative study of the action potential phenomenon. The mathematical interpretation of the biological rules of excitation, introduced by P. Lazarev and developed by N. Rashkevsky and later on by A. Hodgkin and A. Huxley, makes it possible to examine quantitatively the process of excitation of a cell by using mathematical methods.

Around the mid-sixties Gary G. Koch, University of North Carolina, presented an algorithm to determine the compatibility of donor- recipient pairs in organ transplanation. Richard Bellman and his colleagues (The Rand Corporation, California) utilized the non-linear differential-difference equations in the mathematical theories of cancer chemotherapy and in the theories of control mechanisms in the heart lung systems. Bellman and Kotskin and their colleagues prepared a mathematical model to know how the concentration of drug or its by-products build up in the parts of the body. This model simulated the time and space distribution of a drug-injected into the circulatory system. The mathematical approach (asymptotic expansion) was made in the pseudo-steady state hypothesis of biochemical kinetics (enzyme reactions) in the University of Minnesota in the late sixties. The mathematical model of fibrinolysis came into existence to offer the statistical analysis useful in experiments involving drugs with transient effects. The National Health Research Council TNO, The Netherlands, applied a model to data on heartbeat irregularities by using the analysis of expectation density function, probability density function and serial correlation coefficients. Richard Bellman (Los Angeles, California) posed and discussed the general problem of using classical mathematical concepts and conventional general-purpose digital computers to replicate various activites of human brain-mind such as memory, pattern recognition, decision making and learning etc. He also pointed out that the methods of mathematical physics can be used with considerable success to provide understanding of physiological mechanisms in chemotherapy, cardiology, respiratory control, neuro-physiology and in many other areas of medicine.

In the late sixties, the Dartmouth Medical School, Hanover, New Hampshire, described a mathematical model of the passive properties of bladder muscle. The Department of Pharmacology, University of Camerino, Italy, set up a computer programme for the application of a method to locate stereo regular segments in proteins from their amino acid sequences. J. Gani, University of Sheffield, UK, and others employed the probability distribution and other mathematical techniques to study the loss of ineffectivity of spherical influenza virus due to antibody attachment. H.M. Lieberstein, Wichita State University, Kansas, studied the significance of viscous flow properties in the theory of operation of Nephron whose agglomeration may approximately characterize a kidney, by using first order ordinary differential and partial differential equations.

The Canadian Department of Agriculture used mathematical models and techniques for *insect control strategy on a nation-wide-scale. In 1968, the University of Kingston, Ontario, has* shown how a simple mono-molecular biokinetic system can be analyzed on using matrix approach. In 1969, the University of California, Los Angeles, applied the mathematical theory of sequential sampling to gamma scanning in nuclear medicine; also utilized the queuing theory in hospital systems, regarding the surgery cases; presented a computational method for determining the location and size of tumors; fitted the theoretical differential equations to observed experimental kinetic data in drug metabolism; used modern control theory in optimal drug regimens. In Germany, the differential equations were employed in distribution of oxygen partial pressure in two-dimensional tissue supplied by capillary meshes and concurrent and countercurrent systems. L.H. Zetterberg (Stockholm, Sweden) used a linear difference equation in EEG analysis, applying the notion of vector analysis, matrix theory, integrals, correlation coefficients and numerical analysis. Herman Metzger (Germany) applied the differential equations and respective difference equations describing the course of oxygen partial pressure in capillaries and tissues and he solved these equations by the application of the method of successive over relaxation.

Nagumo, Arimoto and Yoshizawa (Japan), in 1962, proposed a third order partial differential equation for a simplified mathematical model of a nerve fibre along with the excitation propagators. In 1969, at University of Tokyo, Japan, a simplified mathematical model of a nerve fibre was described by a semilinear partial differential equation. P.P. Schmidt, University of Georgia, Athens, used the generalized Liouville partial differential equation in the study of the theory of message transport in nerves.

In 1970, at the Neurosensory Laboratory, Pittsburg, Pennsylvania, the researchers made holography and information theory applicable to a description of the physical stimulus for visual perception and the cerebral cortex.

In 1971, Richard Bellman (Los Angeles, California) discussed the asymptotic behaviour of linear differential difference equations for the topics in pharmaco-kinetics and made the application of linear differential equation in some novel types of control processes arising in the study of optimal drug administration. The Department of Nephrology and Mechanics, Haifa, Israel, used a mathematical model for dynamics of dialysis. The integral equations were applied by Mode, Drexel University, Philadelphia, Pennsylvania, in the theory of age-dependent branching processes.

In the mid-seventies in the Department of Zoology, North Carolina State University, Raleigh, the behaviour of a simple aquatic ecosystem with algae, bacteria, daphnia, detritus and usable dissolved organic carbon as its components was studied using random differential equation models. The Centre of Mathematical Statistics and the Institute of Neurology and Psychiatry, Bucharest, Romania, studied the hemodynamic mechanism of cerebral hemorrhage, using the mathematical methods of mechanics of fluids.

The mathematical models have been designed to make experiments to find the optimal methods of administering the drugs and medical treatment. It makes predictions to the cell permeability and reaction rates between drug and cell enzyml molecules. The optimal estimation techniques were applied for measuring blood perfusion in the heart in order to detect and assess coronary diseases and myocardial infarctions, in the University of Texas, Health Science Centre, Dallas. The researchers in A and M University, Texas, applied the Walsh functions and Hadamard matrices for computer-assisted signal processing of EEG data. Fourier analysis also proved very helpful in the signal process of EEG data.

In the beginning of the Eighties, D.D. Do, California Institute of Technology, and P.F. Greenfield, University of Queensland, developed an approximate analytical technique employing a finite integral transform to solve the reaction diffusion problem with Michaelis-Menton kinetics in a solid of general shape. Such problems arise in the formulation of substrate and product material balances for enzymes immobilized within particles; in the description of substrate transport into microbial cells; in membrane transport; in the transfer of oxygen to respiring tissue and in the analysis of some artificial kidney systems. The mathematical analysis of carbon dioxide transport by blood was represented in Lehigh University, Bethlehem, Pennsylvania.

Professor H. Vogel (Germany) and J.N. Ridley (South AFrica) presented the mathematical models for botanical purposes in sunflower heads.

In 1983, International Conference on Mathematics in Biology and Medicine was held in Bari, Italy. The conference objective was to bring together scientists in pure mathematics, biology and medicine in order to exchange ideas on the formulation solution and analysis of mathematical models related to biological issues. The conference proved a grand success, where seventy research papers were presented on "*population genetics and ecology*" (Literature concerned with the issues such as the dynamics of age structured cell populations and Volterra type predator-prey models), "*epidemics*" (Mathematical models of infectious diseases, such as hepatitis B and measles; pros and cons of rubella (vaccination), "*resource management*" (Bayesian methods in resource management and the use of stochastic differential equations in fishery management), "*physiology and medicine*" (Mathematical models useful for interpreting physiological or biochemical data), "*compartmental analysis*" (Mathematical models useful for analysis of staging and age-dependent stochastic systems), "*general mathematical methods*" (the research papers discussing parameter identification for partial differential equation models and stability analysis of differential delay models).

Compartmental analysis is useful in the study of epidemiology, drug kinetics, lipoprotein kinetics, chemical reaction kinetics, metabolic systems, ecosystems and other systems. In compartmental analysis, the dynamic system is separated into a finite number of component parts, called compartments, and flow between compartments is described by ordinary differential equations usually arising from mass-balance considerations.

In the mid-eighties, in Israel Institute of Technology, Haifa, a mathematical method was developed for evaluating the distribution of blood pressure, stresses and strains of the muscle fibres, and motion of the cardiac wall due to the cyclic contraction of the heart. A porous-medium approach was made for modelling heart mechanics.

In the recent past, since the first cases of AIDS (acquired immune deficiency syndrome) were reported, many mathematical models for predicting the spread of the epidemic have been proposed, such as Hyman and Stanley, Los Alamos National Laboratory, New Mexico used deterministic model. Isham V. discussed mathematical modelling of the transmission dynamics of HIV (human immunodeficiency virus) infection and AIDS. Applying the mathematical and statistical devices, Harvard School of Public Health, Boston, Massachusetts, developed discrete-time stochastic model: a generalized chain bionomial model with application to HIV infection. Deterministic models of epidemic spread are tractable mathematically and computationally, while stochastic models are advantageous in order to obtain estimates of variability for the predictions of the number of new infections.

The manufacture of artificial limbs (prosthesis) has been blessed with mathematical techniques to improve the quality upto the ideal state of fulfillment of requirements of disabled persons. The mathematical equations have always played a very important role in all the major chemical species of intracellular and extracellular components of the blood including plasma and homoglobein and in the partial pressures of all the gases in air space. So, one may easily predict the state of a pilot's blood as he goes to higher altitudes.

Recently, orthogonal polynomials have been connected to birth and death processes which are special stationary Markov processes. Birth and death processes have applications to a variety of fields including nuclear physics, spin gas, chemical reactions, population dynamics, genetic models etc.

It is noteworthy that biologists have employed the exponential distribution in radiotherapy; stochastic processes in bacteriology; partial differential equations in spread of epidemics; glucose concentration time curve in the blood during continuous injection of glucose; mathematical models in circulatory system (heart problems), vision, excitation and pulse waves; diffusion in metabolising system, bullisto cardiography, etc. Baye's theorm (probability theory) is used in medical diagnosis to find the probability that a patient has a certain disease. The matrix theory is applied in medical dieting distribution in hospitals. The category theory and topology is applicable in rational biology and biological systems. In the context of population biology and chemical kinetics, the theory of ordinary differential equations, discrete maps, continuous and discrete delay equations, phase plane analysis and partial differential equations are generally used to form molecular and population models. The more recent work of Schaffer and Kot and others have explored the possible implications of chaos on experimental population. Phase resetting and properties of oscillator topology such as "black holes" have been applied very recently in circadian rhythm, neural stimulated response, the cardiac pacemaker and sudden cardiac death.

The collaboration of mathematics and biology has provided a large number of instances of mutual enrichment. A classic example is the case of reaction diffusion systems which motivated the search for biological morphogens and mathematical discoveries about the behaviour of partial differential equations of this type. Other examples include oscillating biochemical reactions and the topology of limit cycles, neural action potential and excitable dynamics, coupled oscillators and phenomena of cardiac wave arrhythmias, chaos and physiological diseases etc.

Since long, mathematical biology has established itself as a subject whose identity is difficult to delineate or to undermine. Its scope has ranged from data analysis, to existence theorems; from large scale computer simulations of physiological systems to an obsession with Lotka-Volterra equations; and from quests for chaos in fluctuating populations to semigroups, circle maps, dynamics on n-dimensional tori and other exotic themes of modern mathematics.

The education pattern in which mathematicians have no knowledge of biology and biologists are unaware of the nature of mathematics, is undesirable in this modern age. Both the different realms of mathematics and biology must be united in order to understand mutual problems and to think over their mutual strategies and line of actions. This is the high demand of the time that bio-mathematicians, bio-statisticians and mathematico-biologists, having the knowledge of both the subjects, are to be produced for the cause of the public welfare in the world.

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