THE ROLE OF MATHEMATICS IN BIOLOGY

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ABSTRACT: Mathematics plays a key role in many disciplines of science, primarily as a mathematical modeling tool. New innovations and developments in physics are by the influence of mathematics. Calculus was invented entirely for the use of physics. The importance of the role of mathematics in physics is understood by the existing discipline “mathematical physics” or "theoretical physics". One can think is mathematics has that same important role or even lesser important role in the field of biology and is mathematics and biology could possibly have anything in common. Even though physics and biology are very different sciences, mathematicians and biologists developed the "mathematical biology" or "biomathematics" as a recent discipline for the mathematical representation in biology to the theoretical and practical applications in biological, biomedical and biotechnology researches. In this paper we study the role played by mathematics in biology and analysis weather a considerable amount of mathematics courses need to be teach for biological science graduates.

Keywords: Mathematics, Biology, Mathematical models, Biomathematics.

1. INTRODUCTION

In early days an attempt was made to establish the mathematical biology as a new discipline, but it did not succeed (Keller,2002). There were initiatives by mathematicians but there were no precedents. For example, theoretical models to describe the spread of diseases had been discussed by Bernouilli and the flow of blood in veins was the uppermost in Euler’s mind when he performed his seminal work on fluid mechanics (Euler,1775).

Mathematical biology or biomathematics is a fast-growing well-recognized and the most exciting modern application of mathematics. This is an interdisciplinary research area with a range of applications in biology, biotechnology and biomedical science. The filed may be referred to as mathematical biology or biomathematics to stress the mathematical side or theoretical biology to stress the biological side. A variety of mathematical techniques are used in mathematical biology to model biological researches. Mathematical areas such as calculus, probability theory, statistics, linear algebra, graph theory, combinatorics, algebraic geometry, topology, dynamical systems, differential equations and coding theory are now being applied in this field.

Many topics from biosciences have been high priority on the global agenda; the fights against cancer and degenerative diseases of the brain, such as Alzheimer's, Parkinson's and ALS and the management of health threats such as AIDS. Society is waiting to get the research results for their better life. The emergence of models and the existence of large data sets that require quantitative analysis in biology gives a great opportunity for mathematics. The existing or already established methods in mathematics can be used to support biological problems but the quantitative analysis of the fundamental problems in bioscience definitely require new ideas and new techniques from mathematics. The most significant biological achievement of the 20thCentury is the identification of the DNA. This work was essentially done by Physicists, Chemists and Crystallographers. There has already been evidence of effective contribution between biology and mathematics. For instance, the modeling of epidemics and the study of signal propagation in nerves are the growing works of differential equations and studies of dynamical system in this century.

There are several biomathematics research groups already established in the departments of mathematics, statistics, computer science and biology and also biostatistics centers around the world. The current size of the mathematical bioscience research groups and researchers is relatively small compared the important and need of mathematics for biological sciences.

2. THE ROLE OF MATHEMATICS TO BIOLOGY

Mathematical biology or biomathematics is a fast growing, well recognized and the most exciting modern application of mathematics. The use of mathematics in biology is important since biology becomes more quantitative. This new discipline has applications in biology, biomedical and biotechnology. The aim of this new discipline is the mathematical representations and modeling of the biological problems using a variety of mathematical theories and techniques. The mathematical biology has both theatrical and practical applications in research on biological, biomedical and biotechnological fields.

One significant work is currently done by Dr. Aver Friedman, distinguished Professor of mathematics and his research team at the Oberlin center for computation and modeling in Ohio State university is to find a cure for cancer (Margaret Putney, 2005). The objective of the research is to use a virus that attacks just the tumor while leaving the healthy cells alone. The cancer which mostly affected by research is a particular type of brain tumor known as glioma. The researchers are trying to find a virus that reproduces fast enough is able to avoid enough of the immune system to reduce the tumor. The researchers of this center found some parameters that would cause the tumor to be reduced. They passed their result to the biologists to create a virus that matches such parameters.

Another contribution of mathematics to biology is a mathematical modeling to address the biological process. The Mathematical Biosciences Institute in Ohio State university works on this work. The institute works on the explosion of biological data which was created by the technology to study biological systems. The data created a need to develop many mathematical models, statistical methods and computational algorithms. The mathematical models needed to encompass the biological process such as neurological and cellular problems. In neurological process, Parkinson's disease is in the center of the modeling work. There are around 1012 neurons in the human brains. To understand properly their relationship with all of the other neurons they proved that the differential equations can be used for the models.

Ecology and evolutionary biology are the dominant fields of mathematical biology. Evolutionary biology has been the subject of extensive mathematical theorizing. Hanna Kokko, theatrical biologists and the professor in the department of biological and environmental science at the University of Helsinki says that much of biology relies on mathematics (Hanna Kokko, 2007).Evolutionary ideas are often complex and the logic of hypothesis proposed should be tested not only empirically but also mathematically.

Another area of specialized research in mathematical biology is the genetic models and various models of the spread of infections. Cancer modeling and simulation, modeling the movement of interacting cell populations, mathematical modeling of the cell cycles are some of the models developed in the discipline of mathematical biology. Molecular set theory was introduced by Anthony Bartholomay. Molecular set theory is a mathematical formulation of the chemical kinetics of bio-molecular reactions in terms of sets of molecules and their chemical transformations. Its applications were developed in mathematical biology and especially in mathematical medicine

Many universities in the western countries offers degrees in the field of biomathematics such as University of St Andrews offers B.Sc. (Hons) in Biology and Mathematics, University of Dundee offers B.Sc.(Hons) in Mathematical Biology, University of Leeds offers B.Sc. in Biology and Mathematics and University of York offers M.Sc. in Advanced Mathematical Biology. These courses consists both mathematics and biology subjects. There is a need to offer a considerable amount of mathematics courses for biology graduates and biology courses for mathematics graduates in Sri Lanka to work in the field of biomathematics.

3. METHODOLOGY

We examine some biological models in which mathematics played major role on the problem. There are more models already developed in biomathematics but we look two simple models for our examination.

Ischemic Wounds

Chronic wounds represent a major public health problem worldwide. To determine therapeutic strategies which help to heal ischemic wounds, a mathematical model were developed by Xue, Friedman and Sen (Avner Friedman, 2010). In this modeling process, a full thickness bipedicle dermal flap was developed first to isolate the blood supply from underneath the flap and from two long edges. One circular wound was developed in the center of the flap (ischemic wound) and another on the normal skin (nonischemic wound). The main variables involved in the wound closure phase of the healing process are several types of blood and tissue cells, chemical signals and tissue density. The model was formulated by using the system of particle differential equations in a partially healed domain.

Figure 1 shows the parts of the wound for modeling. The open wound is the circular region $0 \le r \le R(t)$, the partially healed wound is the annulus $R(t) \le r \le R(0)$ and the normal healthily tissue is the region $R(0) \le r \le L$. They assumed that the wound is circular but small incisions of size δ are made at the boundary $r = L$ with adjacent incisions separated by distance ϵ. Taking $\delta, \epsilon \to 0$ and applying the homogenization theory, each boundary condition $u = u_s$. The derived model is

$$(1-\alpha)(u-u_s) + \alpha \frac{\partial u}{\partial r} = 0.$$

Here α is a measure of ischemia; α near 1 means extreme ischemia. These results are agreement with the experimental results. The model now can be used as a tool to suggest biologically testable hypotheses for improved healing. So this reduces the need for guesswork and time-consuming animal testing.

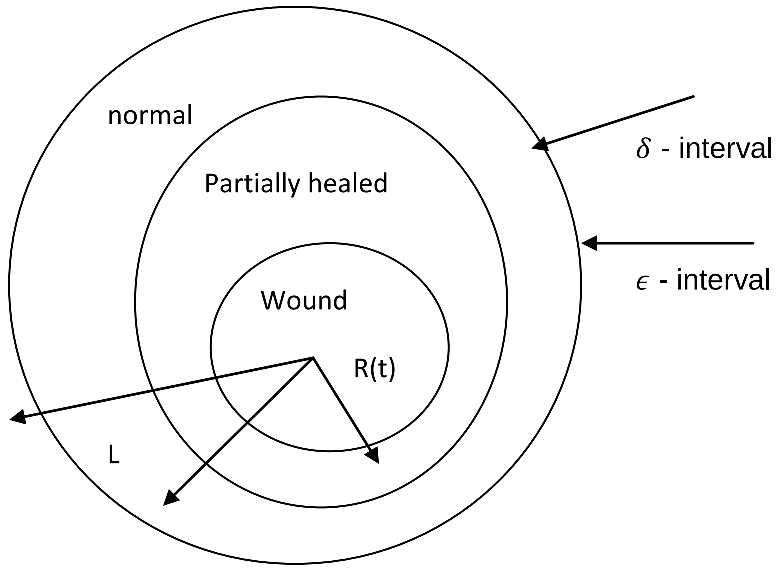

Figure 1. Ischemic Wound

Epidemic models

The study of epidemics has come up with an astonishing number and variety of models and explanations for the spread and cause of epidemic outbreaks (Perelson et al., 1996). A simple but experimentally based model, proposed by Ho et al. (Murray, 2002) for viral production and viral decline was a simple linear first order equation which accounted for viral production and viral decline:

$$\frac{dV}{dt} = P - cV$$

Where P represented a source of viral peptides and $c$was the viral clearance rate. While many factors play a role in the clearance of viral peptides such as immune cells, fluid flow and absorption into other cells, *c* did not distinguish between them. After introduction of the protease inhibitor (the specific type of drug used on the patients) it was assumed that the drug would be completely effective. This means the drug would block all viral production after being introduced. Hence $P = 0$. Therefore, we get the model

$$\frac{dV}{dt} = -cV$$

Which implies that,

$$V(t) = V_0 e^{-ct}$$

Where V_0 is measured as the mean viral concentration in the plasma before the treatment. Due to these models developed by Ho et al. many more models have been developed to the study of HIV.

We can develop four specific models which includes an equation for uninfected T-cells, *T,* productively infected T-cells, T^*(not all infected T-cells produce the virus), infectious viruses, V_1, and noninfectious viruses, V_{N1}. The model consists of the following equations:

$$\frac{dT}{dt} = s + pT\left(1 - \frac{T}{T_{max}}\right) - d_T T - kV_1 T,$$

$$\frac{dT^*}{dt} = (1 - n_{rt})kV_1 T - \delta T^*,$$

$$\frac{dV_1}{dt} = \left(1 - n_p\right)N\ \delta T^* - cV_1,$$

$$\frac{dV_{N1}}{dt} = n_P N\ \delta T^* - cV_{N1}.$$

In the T-cell equation, it was considered the cells destroyed proportional to the number of infected viruses and cells with clearance parameter *k*. In the absence of infection there is a nonzero steady state, T_{s1}. The value for the constants can be calculated by the patients database. Some models have assumed that the T-cells do not change dynamically during the first weeks of treatment and hence we set $T = T_0$, a constant. However, after antiretroviral therapy is initiated some recovery of T-cells is observed and patient data presented by Ho et al (Ho et al., 1995) suggested that over a period of weeks the recovery of T-cells can be described by either a linear or exponential function of time with no statistically significant difference between the two functions over that time period. T-cells replacement can be due to the source s, which incorporates the generation of new cells in the thymus or to proliferation of cells. If source s is the major mechanism of T-cell replacement, we can then approximate the T-cell dynamics by

$$\frac{dT}{dt} = c - d_T T$$

or equivalently

$$T(t) = T_0 + at$$

where a is a constant.

More analysis can be done through these models and can develop more accurate models using the biological concepts and mathematical theories. Development of more accurate models need the knowledge in both biology and mathematics. One subject knowledge is not sufficient as this is a practical biological problem which can be solved mathematically.

Biological waves: single-species models

There is a vast number of phenomena in biology in which a key element to a developmental process seems to be the appearance of a travelling wave of chemical concentration, mechanical deformation, electrical signal and so on. The widespread existence of wave phenomena in the biomedical sciences which require the study of travelling waves in depth and of the modeling and analysis involved is mentioned in many places. For example, the introductory text on mathematical models in molecular and cellular biology edited by Segal (Segal, 1980) deals with some aspects of wave motion. Estimation of diffusion coefficients for insect dispersal in interacting populations in now studied with care and supplication.

The standard diffusion equation in one space dimension, is of the form

$$\frac{\partial y}{\partial t} = D\frac{\partial^2 y}{\partial t^2}$$

where D is the diffusion coefficient. When reaction kinetics and diffusion are coupled, travelling waves of chemical concentration exists and can effect a biochemical change very much faster than straight diffusion process given by

$$\frac{\partial y}{\partial t} = f(u) + D\frac{\partial^2 y}{\partial t^2}$$

where u is the concentration, $f(u)$ represents the kinetics and D is the diffusion coefficient. This model further developed in the areas of ecology and developmental biology which belong to important areas where modeling has played a significant role.

4. RESULTS AND DISCUSSION

The above example models show the role played by mathematics in biological problems. They clearly indicated that a deep knowledge in both mathematics and biology is very important for the development of realistic models. A Continuous discussion between biologist and mathematicians is also needed during the modeling process. When the models are formulated by mathematicians, they will be passed to biologists for testing in real situations. During the testing process, factors involved in the problem will be examined using the model and patient data. So the factors will be evaluated using the patient data and model and compared. Any assumptions made during the modeling process will also be tested with patient data or realistic conditions. Improvement suggestions will be passed from biologists to mathematicians for development of better models. This process will continue for a number of cycles until a better model is formulated by both biologists and mathematicians. We should note that when biologists pass their requirements to mathematicians, the mathematicians should have knowledge in biology to understand the biologists' request. Similarly, when the mathematicians developed a model, the biologists should have mathematics knowledge to understand the model.

It clearly shows that knowledge in both mathematics and biology is very important to solve biological problems. This also indicated the importance of a discipline which is a combination of mathematics and biology. Since this new discipline deals with real problems and solve them in a realistic way, this new discipline, biomathematics, becomes popular among biologist and mathematicians.

5. CONCLUSION

The great alliance between mathematics and physics is well recognized universally. Both disciplines are supporting each other. There are areas in biology which have advanced by mathematics, such as computational neuroscience, population dynamics, ecology, spread of disease and phylogenomics. In future, the mathematics will be the future frontier of biology and biology is the future frontier of mathematics. Considering this new trend, important mathematics courses should be included in biology curriculum to understand the applications of mathematics and also a considerable number of biology courses should be included to mathematics curriculum to understand the biological problems. The new discipline, biomathematics, should be introduced in our undergraduate and postgraduate curriculum to produce our graduate with the latest research knowledge in biological stream.

6. REFERENCES

AVNER FRIEDMAN (2010) What is mathematical biology and how useful is it? Notices of the AMS, pp. 851-857.

EULER. L. (1775) Principia pro motosanguinis per arteriadeterminando. Quoted in S. J. Sherwin, V. Franks, J. Peiro and K. Parker, *One-dimensional modelling of a vascular network in space-time variables,* J. Eng. Math., 47 (2003). pp. 217-250.

HANNA KOKKO (2007) Modelling for Field Biologists and Other Interesting People, Cambridge University Press.

KELLER. E. F. (2002) Making sense of life: explaining biological developments with models, metaphors and machines, Harvard University Press, Cambridge.

MARGARET PUTNEY (2005) Mathematics + Biology = ?, The Oberlin Review.

MURRAY. J.D. (2002) Mathematical Biology-I An Introduction, Interdisciplinary Applied Studies, Vol.17, Springer.

PERELSON. A.S., NEUMANN. A.U., MARKOWITZ. M, LEONARD. J.M, and HO. D.D. (1996) HIV-1 dynamics in vivo: Virion clearance rate, infected life-span and viral generation time, Science, 271. pp. 1582-1586.

HO. D.D, NEUMANN. A.U., PERELSON. A.S, CHEN. W, LEONARD. J.M, and MARKOWITZ. M, (1995) Rapid turnover of plasma virions and CD4 lymphocytes in HIV-1 infection, Nature, 373, pp. 123-126.

SEGAL. L.A., editor. (1980) Mathematical Models in Molecular and Cellular Biology, Cambridge University Press.