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## Mathematics Serve to Orchestrate the Progression of Studies In Biological Sciences: Overview on Occasion of April, the Mathematics Awareness Month

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### ABSTRACT

The mathematics and biology are the interdisciplinary approaches in the field of scientific research. Both, mathematics and biology deserve a wide range of applications. Mathematical biology or biomathematics is the study of mathematics for biology. One can derive the quantitative genetics through consideration of infinitesimal effects at a large number of gene loci, together with the assumption of linkage equilibrium or quasi-linkage equilibrium. Ronald Fisher made the intensive work on fundamental advances in statistics (Example: Analysis of Variance). This achievement by Ronald Fisher was through his work on quantitative genetics. The phylogenetics is one more important branch of population genetics that led to the extensive development of Biological sciences through Mathematics. The Phylogenetics is the branch dealing with the reconstruction and analysis of phylogenetic (evolutionary) trees and network based on inherited characteristics. Assumptions on the "Constant Population Size" belongs to many "Population Genetics" models. The population dynamics is treating the "Variable Population Size" as absence of genetic variation. History of such type of work goes back to the 19<sup>th</sup> century. Even as far as 1798. In 1798, Thomas Malthus formulated the first principle of population dynamics. This principle later became popularize as the "Malthusian Growth Model". Alfred J. Lotka, in 1910 proposed the model of autocatalytic chemical reactions. Vito Volterra tried his best to extend this work and titled as "Lotka - Volterra Predator-Prey Equations". Basically, Vito Volterra was Mathematician. The mathematical epidemiology is the study of infectious disease affecting populations. Upto some extent, the "Population dynamics" use to overlaps

mathematical epidemiology. The mathematics and Biology, both are serving a lot to orchestrate the progression of the global research.

**Keywords:** Biomathematics, Quantitative Genetics; Population Dynamics; Supercomplex Mechanisms

## 1. INTRODUCTION

Mathematics is with a crucial role in any education system. Mathematical and theoretical biology are the interdisciplinary scientific research fields with a range of their applications. The branch is sometimes called “Mathematical Biology” or “Biomathematics” to stress the mathematical side. It may also called as “Theoretical Biology” to stress the biological side. The “Theoretical Biology” use to focus more on the development of theoretical principles for biology. “Mathematical Biology” focuses on the use of mathematical tools to study biological systems. According to Longo and Soto (2016) and *Montévil, et al* (2016), even though the two terms “Mathematical Biology” and “Theoretical Biology” are sometimes interchanged, the concept remains one and the same.

The sole aim of “Mathematical Biology” is mathematical representation, treatment and modeling process expected in Biology. This is achieved through using techniques and tools of applied mathematics. “Mathematical Biology” has both theoretical and practical applications in research in the fields of biology, biomedical science and biotechnology. The biology use to explain the process of digestion in larval instars of silkworm, *Bombyx mori* (L) for example. The “Mathematical Biology” is expecting amount of food consumption and utilization by the tissue. “Mathematical Biology” explain in a quantitative manner, with appropriate signs and measurements (with meaningful correlation). Therefore, the biological systems can be better simulated, and hence properties can be predicted that might not be evident to the experimenter. According to Robeva, Raina (2010), Mathematical Biology employs many components of mathematics and has contributed to the development of new techniques.

There is application of Mathematics in Biology since the 19<sup>th</sup> century. Fritz Müller (Birth: 31 March 1821 – Death: 21 May 1897) (Original name: Johann Friedrich Theodor Müller) described the evolutionary benefits of adaptation of organism to environment. The adaptation of organism to environment was popularized as “Müllerian mimicry” in 1879. The account of “Müllerian mimicry” is notable for being the first use of a mathematical argument in evolutionary ecology. It explain “How powerful the effect of natural selection would be”. It also highlights on “effects of population growth” The Mathematical Biology argued that population growth would be "geometric" while resources (the environment's carrying capacity) could only grow arithmetically (Mallet James, 2001).

One founding text is considered to be “On Growth and Form” (1917) by D'Arcy Thompson (Ian Stewart, 1998), and other early pioneers include Ronald Fisher, Hans Leo Przibram, Nicolas Rashevsky and Vito Volterra (Evelyn Fox Keller, 2002). 1960 is the year which shows rapid growth of the “Interest in Bio-mathematics” .

Followings are some possible reasons for rapid growth of the “Interest in Bio-mathematics”:

- The genomics, the newly launched area made rich collection of the data in the form of “Information”. The genomics revolution is difficult to understand without the use of mathematical analytical tools.
- The chaos theory and the other recent development of tools in mathematical analysis to help to learn complex, non-linear mechanisms in biology.
- The calculations and the simulations were not possible before the computer era. The computers made increase in computing power. The computers allowed calculations and simulations not previously possible.
- An increasing interest in in silico experimentation due to ethical considerations, risk, unreliability and other complications involved in human and animal research

## **2. RESEARCH AREAS IN BIOINFORMATICS**

The biomathematics deserve wide range of applications in research. There are several areas of specialized research in mathematical and theoretical biology (Baianu, et al, 2006). In addition, there are external links to related projects in various universities are concisely presented in the following subsections, including also a large number of appropriate validating references from a list of several thousands of published authors contributing to this field. mechanisms. The results of such and other interactions may only be understood through a combination of mathematical, logical, physical, chemical, molecular and computational models. Many of the included parameteres are characterised by highly complex, nonlinear, and supercomplex.

Generally, the biomathematical research is carried out through collaboration between mathematicians, biomathematicians, theoretical biologists, bioinformaticians, biostatisticians, physicists, biophysicists, biochemists, bioengineers, engineers, biologists, physiologists, research physicians, biomedical researchers, oncologists, molecular biologists, geneticists, embryologists, zoologists, chemists, etc. This is because of wide diversity of specific knowledge involvement.

## **3. EVOLUTIONARY BIOLOGY**

Johann Friedrich Theodor Müller (31 March 1821 – 21 May 1897), better known as Fritz Müller wrote *Für Darwin* in 1864. In this book, he argued that Charles Darwin's theory of evolution by natural selection was correct, and that Brazilian crustaceans and their larvae could be affected by adaptations at any growth stage (Muller Fritz, 1978). Traditionally, the dominant areas of mathematical biology are the ecology and evolutionary biology. There is extensive mathematical theorizing in evolutionary biology. The traditional approach with reference to population genetics is supposed to be complications from genetics in this area. In the population geneticists, it is considered that, “The appearance of new alleles by mutation, the appearance of new genotypes by recombination, and changes in the frequencies of existing alleles and genotypes at a small number of gene loci”. When infinitesimal influences at a large number of gene loci are considered, together with the assumption of linkage equilibrium or quasi-linkage equilibrium, one derives quantitative genetics, the mathematical

vision for biology. According to Ronald Fisher (1928), fundamental advances in statistics correlates the mathematics and biology through the study areas such as analysis of variance, via his work on quantitative genetics. Phylogenetics is another important branch of population genetics. It lead to the extensive development of coalescent theory is phylogenetics. Phylogenetics is dealing with the reconstruction and analysis of phylogenetic (or evolutionary) trees and networks based on inherited characteristics (Charles Semple, 2003). Traditional population genetic models is dealing with alleles and genotypes, and are frequently stochastic.

According to population genetics models, population sizes are constant. The variable sizes of the population, often in the absence of genetic variation, are treated by the field of population dynamics. The history of work in this area goes back to the 19<sup>th</sup> century. The supportive documents are even as far as 1798 when Thomas Malthus formulated the first principle of population dynamics. Later, the formulation of Thomas Malthus became known as the “Malthusian Growth Model”. The Lotka–Volterra predator-prey equations are another famous example. Population dynamics overlap with another active area of research in mathematical biology: mathematical epidemiology, the study of infectious disease affecting populations. Various models of the spread of infections have been proposed and analyzed, and provide important results that may be applied to health policy decisions.

John Maynard Smith and George R. Price developed the evolutionary game theory. According to this theory, the “Selection acts directly on inherited phenotypes, without genetic complications”. Further, this approach has been mathematically reshuffled to produce the field of adaptive dynamics.

#### **4. THEORY OF COMPUTER MODELS AND AUTOMATA**

A document on the “Theory of Computer Models and Automata” summarizes an extensive amount of published research in this area up to 1986 (Witten, 1986; Lin, 2004). This attempt tried it’s best to include subsections in the following areas: The computer modeling in biology and medicine; The arterial system models; the neuron models; the biochemical and oscillation networks; the quantum automata; the quantum computers in molecular biology and genetics; the cancer modeling (Baianu, 2004); the neural nets; the genetic networks; the abstract categories in relational biology (Kainen, 2005); the metabolic-replication systems; the category theory applications in biology and medicine; the automata theory; the cellular automata; the tessellation models and complete self-reproduction; the chaotic systems in organisms; the relational biology and organismic theories (Baianu, 1987). The growing importance of molecular biology boosted area of “cell and molecular biology”. Mechanics of biological tissues (Ray Ogden, 2004):

- Theoretical enzymology and enzyme kinetics
- Cancer modelling and simulation (Oprisan, et al , 2006)
- Modelling the movement of interacting cell populations (Wolkenhauer, 2004)
- Mathematical modelling of scar tissue formation
- Mathematical modelling of intracellular dynamics (Kuznetsov and Avramenko, 2009).

- Mathematical modelling of the cell cycle (Noe, et al, 2017)
- Modelling of arterial diseases cycle (Noe, et al, 2017)
- Multi-scale modelling of the hear cycle (Noe, et al, 2017)
- Modelling electrical properties of muscle interactions, as in bidomain and monodomain models

## **5. MOLECULAR SET THEORY: MATHEMATICAL FORMULATION FOR BIOCHEMICAL KINETICS**

The Molecular Set Theory (MST) was introduced by Anthony Bartholomay. It is a mathematical formulation of the wide-sense chemical kinetics of biomolecular reactions in terms of sets of molecules and their chemical transformations represented by set-theoretical mappings between molecular sets. The applications of Molecular Set Theory (MST) were developed in mathematical biology and especially in mathematical medicine. In a more general sense, MST is the theory of molecular categories defined as categories of molecular sets and their chemical transformations represented as set-theoretical mappings of molecular sets. It has also contributed to biostatistics and the formulation of clinical biochemistry problems in mathematical formulations of pathological changes, biochemical changes of interest to Physiology, changes in Clinical Biochemistry and Medicine (Noe, et al 2017). The term “Model” is often used synonymously with the “Corresponding System of Equations”. In the Molecular Set Theory (MST), there is conversion of model of a biological system into a system of equations. This system of equation use to help to solve and find the solution of the equations. This is employed by either analytical or numerical means. Each and every step in the solution explains “How the biological system behaves either over time or at equilibrium”.

Different types of behavior or the factors of biological systems affect on the corresponding system of equations. There are many different types of equations and the type of behavior that can occur is dependent on both the model and the equations used. The model often makes assumptions about the system. The equations may also make assumptions about the nature of what may occur (Noe, et al, 2017).

Due to the recent significant modifications in performance, the computer accelararetes the model simulation based on various formulas. The Bio-Math-Modeler websites can carry out simulations and display charts interactively on browser. The earlier phases of mathematical-biology was dominated by mathematical-biophysics. The mathematical-biophysics described as the application of mathematics in biophysics. It is generally, involving specific physical or mathematical models of systems, components or compartments in biosystems.

## **6. BIOLOGICAL ORGANIZATION**

The aim of theoretical approaches to biological organization is to understand the interdependence between the parts in the body of organisms. These approaches emphasize the circularities that these interdependences lead to. Theoretical biologists developed several concepts to formalize the concept of “Interdependence of various organs in the body”.

Abstract Relation Biology (ARB), for example, is concerned with the study of general, relational models of complex biological systems. The ARB, usually abstracting out specific morphological, or anatomical, structures. Some of the simplest models in ARB are the Metabolic-Replication (MR) and Relational models. The Metabolic – Replication (M R) was the systems introduced by Robert Rosen in 1957-1958 as abstract. The relational models was introduced by Rosen Robert in 2005. The relational model was to introduce the concept of cellular and organismal organizations. The other theoretical approaches to biological organization include the notion of autopoiesis developed by Maturana and Varela, Kauffman's Work-Constraints cycles, and more recently the notion of closure of constraints (Maturana and Varela, 1973 ; Maturana, H. (2002).

The algebraic biology is also known as “Symbolic-Systems-Biology”. It applies the algebraic methods of symbolic computation to the study of problems in biology, especially in genomics, proteomics, analysis of molecular structures and study of genes (Michael P Barnett, 2005).

## **7. CELL CYCLE : IDEAL EXAMPLE MODEL FOR BIOINFORMATICS**

Sequential and repetitive events in the life of the cell may be called as cell cycle. It is the series of events that take place in a cell leading to its division and duplication through its DNA (DNA replication) to produce two daughter cells. In prokaryotes (ex. bacteria), there is no nuclear membrane to keep the nuclear material separate from cytoplasm. That is to say the nuclear material and ctoplasmic material are mixed with each other. The the cell cycle in prokaryotes is divided into the the periods, may be entitled: Period: “B”, Period: “C”, and Period: “D” periods. The Period: “B” extend from the end of cell division to the beginning of replication of DNA. The replication of DNA occurs during the Period: “C”. The Period: “D” refers to the stage between the end of the replication of DNA and the splitting of the bacterial cell into two daughter cells (Michael P Barnett, 2005). In eukaryotes, the cell is with a nucleus. The eukaryotic the cell cycle is divided into three periods or phases: interphase (I), the mitotic (M) phase and cytokinesis (C). During interphase (I), there is growth of cell. The cell is accumulating nutrients needed for the cell division. There is preparation of cell itself for cell-division and duplicating its DNA. During the mitotic (M) phase, the chromosomes duplicate and separate. During the final stage, cytokinesis (C), the chromosomes separates followed by cytoplasmic division yielding the daughter cells. To ensure the proper division of the cell, there are control mechanisms known as cell cycle checkpoints.

The cell-division cycle deserve vital virtualness. The cell division is the process by which a single-celled fertilized egg (Zygote) develops into a mature organism. The cell division is required for the growth and life of organs in multicellular organisms. There is renewal of many parts of the body through the process of cell division. Soon after cell division, the daughter cells enters in the interphase of a new cell cycle. Each phase of the cell cycle significant set of specialized biochemical process. The misregulation of cell cycle in eukaryotic organisms may leads to cancers. Most possibly, the cell cycle is a good example of a mathematical model. It deals with simple calculus but gives valid results. Two research groups. The “Generic Eukaryotic Cell Cycle Model” is representing a particular eukaryote depending on the values of the parameters. It is demonstrating the “Idiosyncrasies” of the individual cell cycle.

Idiosyncrasies are formed through to different protein concentrations and affinities. The underlying mechanisms of diosyncrasies formation are conserved (Csikasz-Nagy, et al., 2006).

In deterministic process, models show the change in time (dynamical system) of the protein inside a single typical cell. In stochastic process, the model is describing a statistical distribution of protein concentrations in a population of cells is called a stochastic process.

For the purpose to get mathematical equations, an iterative series of steps include:

- I. The observations of several models.
- II. Formation of Consensus Diagram based on observations of several models.
- III. Selection of appropriate kinetic Laws or the principles.
- IV. Establishment of Mathematical Equation (may be in the form of diffedential equation). For example: The rate kinetics for stoichiometric reactions, Michaelis-Menten kinetics for enzyme substrate reactions and Goldbeter–Koshland kinetics for ultrasensitive transcription factors.
- V. Fitting the parameters of the equations (rate constants, enzyme efficiency coefficients and Michaelis constants). This is to match observations. When they cannot be fitted, the kinetic equation is revised and when that is not possible the wiring diagram is modified.
- VI. Validation of the equation using observations of both, in laboratory readings and field readings.

For the purpose to fit the parameters, the differential equations must be studied. This can be done either through simulation or through analysis. In a simulation, there is calculation of progression of the system through the use of given a starting vector (list of the values of the variables). It is followed by solving the equations at each time-frame in small increments.

In the analysis, there is investigation of the behavior of system (depending on the values of the parameters and the variables) through the use of properties of the equations. A system of differential equations for example, can be represented as a vector field, where each vector described the change (in concentration of two or more protein) determining where and how fast the trajectory (simulation) is heading. The fields of Vector can have several special points, which include: a stable point, called a sink, that attracts in all directions (forcing the concentrations to be at a certain value), an unstable point, either a source or a saddle point, which repels (forcing the concentrations to change away from a certain value), and a limit cycle, a closed trajectory towards which several trajectories spiral towards (making the concentrations oscillate).

Through the use of bifurcation theory, it is possible for better representation of the biological data. It handles the large number of variables and parameters. In a biochemical reaction, there is a special steady-state points at certain values of a parameter. These parameters are represented by a point. Once the parameter passes a certain value, it yield a qualitative change. This qualitative change, at certain point of known variable (or parameter) is nothing but a bifurcation. In a cell cycle, nature of the space changes, with profound consequences for the protein concentrations. In terms of mathematics, cell cycle has phases like G.1 and G.2.

The level of cyclin in each of the phase controls the process of cell cycle. Through the stable point, mass of the cell, controls cyclin levels. In the Synthetic phase and M phase, the concentrations change independently. It is impossible for the system to go back to the previous level. This because, at the current mass the vector field is profoundly different and the mass cannot be reversed back through the bifurcation event. The event of bifurcation is responsible for making a checkpoint irreversible. In particular, in S phase and M phase, the checkpoints are regulated by means of special bifurcations called a Hopf bifurcation and an infinite period bifurcation.

## **8. CONCLUSIONS**

The study of mathematics for biology is sometimes called mathematical biology or biomathematics to stress the mathematical side, or theoretical biology to stress the biological side. One can derive the quantitative genetics through consideration of infinitesimal effects at a large number of gene loci, together with the assumption of linkage equilibrium or quasi-linkage equilibrium. Ronald Fisher made The intensive work on fundamental advances in statistics (Example: Analysis of Variance) belong to Ronald Fisher. This achievement by Ronald Fisher was through his work on quantitative genetics. The phylogenetics is one more important branch of population genetics that led to the extensive development of Biological sciences through Mathematics.

The Phylogenetics is the branch dealing with the reconstruction and analysis of phylogenetic (evolutionary) trees and network based on inherited characteristics. Assumptions on the “Constant Population Size” belongs to many “Population Genetics” models. The population dynamics is treating the “Variable Population Size” as absence of genetic variation. History of such type of work goes back to the 19<sup>th</sup> century. Even as far as 1798. In 1798, Thomas Malthus formulated the first principle of population dynamics. This principle later became popularize as the “Malthusian Growth Model”. Alfred J. Lotka, in 1910 proposed the model of autocatalytic chemical reactions. Vito Volterra tried his best to extend this work and titled as “Lotka - Volterra Predator-Prey Equations”. Basically, Vito Volterra was Mathematician.

The mathematical epidemiology is the study of infectious disease affecting populations. Upto some extent, the “Population dynamics” use to overlaps mathematical epidemiology. Conclusively enough, intervention (correctly, the titre) of mathematics serve to orchestrate the progression of studies in biological sciences.

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