**Mathematics in Physiological System Modelling**

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**ABSTRACT**

Mathematics is extensively used in designing physiological modelling . There exists a long and rich history of mathematical modelling in physiology. Mathematical modelling basically refers to creating a mathematical representation of a real life condition .Physiological modelling is similarly the creation of a mathematical representation of a physiological system. A huge number of mathematical models for many aspects of human physiology and pathology have been produced in recent decades. Understanding the connections between the parts of a complicated system may be accomplished with the use of mathematical models. In the biological context, mathematical models aid in our understanding of the intricate web of relationships among the various components (DNA, proteins, enzymes, signaling molecules, etc.) in a biological system. This improved understanding allows us to predict the behaviour of the system in a diseased state. Our understanding of several intricate biological systems, including enzyme kinetics, metabolic networks, signal transduction pathways, gene regulatory networks, and electrophysiology, has improved because to mathematical modelling. The study of biological systems has grown even more reliant on computational approaches and mathematical modelling as a result of recent developments in high throughput data production techniques.

1. **INTRODUCTION**

In physiology, mathematical modelling has a long and illustrious history[1]. It is helpful to quickly explain the general modelling technique before getting into a discussion of how models have advanced our understanding. Mathematical modelling starts with a well-formulated hypothesis based on prior findings, just like experimental research do. In actuality, the mathematical model is best understood as a quantitative depiction of the main idea. For instance, Otto Frank developed a mathematical model of the arterial pulse in the late nineteenth century [2]. Over the years, similar mathematical techniques to comprehend the mechanical characteristics of the circulation have persisted, as Bunberg and colleagues recently reviewed [3]. Hodgkin and Huxley's foundational study on the development and propagation of neural action-potentials was published around the middle of the last century [4], from which cardiac electrophysiology models quickly developed and spread [5]. Mathematical modelling in physiology quickly transitioned from analytical techniques to computational implementations of governing equations and their simulation in order to take use of the newly emerging capability of first analog and subsequently digital computers. The size of the problems addressed and examined was able to grow as a result of this progress, For instance, Arthur Guyton and his collaborators created an elaborate representation of fluid-electrolyte balance in the late 1960s that still impresses today due to the range of physiology it covers[5].

Since the time of Guyton's original research, physiological modelling has moved from specialized and frequently single-purpose computers to the researcher's desktop, as even small-scale computer clusters can be assembled at comparatively little expense. This is due to the widespread availability of relatively low-cost, high-performance computing power and storage capacity. Numerous quantities of biological, biomedical, and even clinical data may now be collected and saved as part of specialized research initiatives or during normal clinical patient treatment thanks to technical developments in computer power and digital storage media. The need to simultaneously link observed data stream characteristics mechanistically to the properties of the system under study, and potentially in real-time as required by some clinical applications [6], is even more urgent. If this is not done, the vast amounts of biomedical data will not be translated into a better understanding of the biological systems themselves. This link is the mechanistic, mathematical and computational modelling of biological systems at all physiological length and time scales, as envisioned by the Physiome project [1,7, 8].

1. **MECHANISTIC MATHEMATICAL PHYSIOLOGICAL SYSTEM MODELS**

Mechanistic mathematical models represent the amount of knowledge we now have about the functional relationships that control the overall behavior of the system under study. By putting our understanding of physiology into the context of dynamical systems (deterministic or stochastic), we make it possible to make exact quantitative predictions and compare them to the outcomes of carefully selected trials. Mechanistic mathematical models frequently enable us to investigate a system in much greater depth than is feasible in experimental research and can thus help in determining the reason behind a certain discovery [6]. Mathematical models and experiments work very well together when completely integrated into a scientific program since the presence of one considerably increases the value of the other: In addition to illuminating experimental findings, allowing for discrimination between competing scientific hypotheses, and aiding in experimental design, models depend on experiments for the definition and improvement of parameter values. [6]. Numerous applications of mathematical modelling have been made to shed light on the molecular and ionic processes underlying both inherited and acquired disease. Dr. Yoram Rudy's lab's work has been essential to this attempt. Notably, the Luo-Rudy dynamic model and its variations continue to rank among the most often mentioned models of cardiac action potentials and are frequently used to explore the fundamentals of cardiac electrophysiology.

[9-13]. Additionally, investigations utilizing these models have shown the effectiveness of computational methods in producing fresh mechanistic insights into cardiac arrhythmia [14-17]

1. **MATHEMATICAL MODELLING OF THE REPRODUCTIVE SYSTEM**

Men and women differ significantly in many organ systems, including the structure of the brain, the functioning of the immunological and stress systems, as well as the metabolic and cardiovascular processes; They also differ in reproductive system and reproductive behaviours [18]. The creation of successful sex-based treatments depends on a thorough knowledge of how these sex variations affect health and disease. A renewed focus on computational physiology will be necessary to enable the integration and analysis of enormous amounts of life-science data. This is because of the recent explosion of biological, biomedical, and clinical data at all levels of organization, from the cellular to the organismic. The knowledge of sex variations in health and illness has the potential to be facilitated and advanced by mathematical modelling. Many people are also aware of the disparities in physical composition between the sexes: men usually have proportionately higher bone mass, muscular mass, and body fat percentage than women.

The structural/morphological variations between adult males and females for most (if not all) organ systems are underappreciated yet can have a big influence on physiological function. The variations in both the genders can be well created using mathematics and the physiological system thus designed may be utilized for various research and studies. Mathematical models are the new upcoming tools for enriching our knowledge of the reproductive system and to simplify the complexities of the reproductive system [19]. The modelling using mathematics also helps us to simplify and compare and analyse and understand the variations in the physiology of the male and the female physiological systems [20]. Studies show that the Laplace equation is applied to the event of follicle rupture is beneficial to interpret the simultaneous impact of several factors that lead to bursting of the follicle i.e., ovulation in female. On the other hand, the dynamics of the transport of the gamete by peristaltic analysis applied to the beat of the cilia lining the female oviduct has been interpreted. The metachronal wave which is generated in the wall of the vas deferens in male is known to contradict peristalsis and hence becomes the dominating factor in spermatozoa transport. Similarly, mathematical modelling is applied to understand the biomechanical significance of the forces associated in the mechanics of sperm-egg interactions and fertilization[20]. Von Foerster's equation is used to formulate a fertilization index which accounts for the reserve of epididymal spermatozoa and also the numbers of spermatozoa present in a specific ejaculation[20,21].

1. **MATHEMATICAL MODELLING OF THE DEVELOPMENTAL BIOLOGY**

Studies show that mathematical modelling can be successfully used to analyses and understand the various complex aspects of developmental biology[22].Application of generalised Hook's law in order to get the displacements for specific load conditions at the time of moulding of fetal head is known [20].The use of mathematical in developmental biology is evolving daily. Mathematical principles are used to understand the basic principles which drive morphogenesis in embryo developmental process. Studies report use of mathematical modelling of gastrulation in the embryo of chick for understanding the events of morphogenesis. The study reveals extensive utilization of mathematical formulations in addressing the problem of interplay between the dynamics of the gradients of morphogenesis and the cellular movements [22]. Use of various mathematical models are also reported in studying the developmental cycle of *Dictyostelium discoideum*[22]. Studies show that differential equation models are the best ones in studying developments of embryo[23]. Segment polarity network in the early development of the embryo of *Drosophila melanogaster* is interpreted using mathematical modelling. Simple models are designed and used to understand the complex process of segment polarity network[24].Whole embryo modelling of early segmentation in the *Drosophila melanogaster* has been used to identify crucial and robust and fragile expression domains[24]. Diffusion models are also in extensive use and helps in forming hypotheissi about the properties of morphogen in embryos of various species [22].

1. **MATHEMATICAL MODELLING OF THE NERVOUS SYSTEM**

The development of neurons is a very complex process. Mathematical modelling and numerical simulation is widely applied in interpreting the complex processes involved in initiation, elongation, axon formation and branching of the neurites [25]. Thus mathematical modelling is highly beneficial in studying the process of morphological development of neurones. Differential equations are widely applied for understanding various neural events including morphological development of the nervous system[25]. Some of the mathematical models that are used in studying neuroscience and in understanding the nervous system are models of neurons and synapses, models of memory, models of sleep and wakefulness, models of disorders and diseases etc.,.

Mathematical modelling of the neural network has been an interesting topic of research since many years. The model not only helps us to understand and study the electrical activities of the neural network but also application of these interpretations has helped us to develop advanced tools like neurorobotics for better and much efficient exploration of the nervous system. Various mathematical models have been designed for different types of neural disorders. Some of the models mimic a particular neural disease condition and is used to understand the underlying mechanism of the disease and is also used to design the treatment regimes and therapy for the same [26].Mathematical models of the nervous system have also been used to address critical conditions of the nervous system and the brain as in hydrocephalous[27].

1. **MATHEMATICAL MODELLING OF THE ENDOCRINE SYSTEM**

Mathematical models of endocrine system coupled with carefully designed experiments helps to understand in details the complex processes and endocrine regulations various levels of organisation. Using novel mathematical models in which the pancreas is being considered as a network of beta cells, the process of rhythmic secretion of insulin is studied [28]. Complex regulatory mechanisms underlying various events of stress, metabolism and reproductive axes have been studied in details using mathematical modelling.Mathematical modelling has been used to reveal the mechanism of exhibition of normal ultradian pulsatility by glucocorticoid. The mechanism of how glucocorticoid responds to stressors like inflammation is also revealed using mathematical modelling[29].Mathematical modelling of the immune regulation by glucocorticoid is used to understand various aspects and mechanisms involved in the immune regulation by glucocorticoid[29]. A possibility of dose dependent suppression of the anti-tumor immune response by glucocorticoid is revealed by the mathematical modelling study[29]. New strategies of ovarian stimulations are also revealed by using mathematical modelling and simulations [30].Statistical models have also been

designed and are in use to address different outcome criteria of IVF [31].

1. **MATHEMATICAL MODELLING OF DIGESTIVE SYSTEM**

Mathematical modelling is in extensive use in understanding and interpreting the various processes involved in digestion. Mathematical model is reported to be used to study the process of digestion and absorption in pig[32].Mathematical model is also used to describe regulation of digestion. The model is based on data which were acquired from the analysis of more than twelve hundred sources of experimental observations reported on digestion performed on dogs [33]. A mathematical model of digestion of the small intestine is also reported. The model is used to understand and describe the different aspects of digestion. These include primarily the transport of food bolous along the digestive tract, degradation of the food depending on the enzymes and the physical conditions etc.,. Various numerical computations are used for the purpose [34].Mathematical modelling is also used to understand the mechanism and details of food hydrolysis [35].

1. **CONCLUSION**

To concise the topic, physiological phenomenal are having specific inputs, central integrators and outputs. These throughputs can be computed by mathematical expressions. Based on these expressions laboratory based computational physiology models can be devised having wide range of applications in clinical and non clinical studies providing an insight into the complex working mechanisms in in vivo systems. These models have fascinating approaches in understanding the various patters of developmental aspects in human, sexual dimorphic patterns in brain functioning, metabolism, energy homeostasis, cardiovascular functions, stress and immune responses. Finally mathematical modelling thus explores the clues to the mechanisms of development of diseases and pathophysiological conditions in males and females by integrating the copious amount of observed data, simulation, exploration of hypothesis, parameter estimation. Various physical and mathethemetical laws like differential equations, Laplace's transformations, computer assisted techniques contributes a lots to development of drugs, therapeutic regimens and management of diseases which is a great stride towards a satisfactory living of mankind in the 21st generation.

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