



# MATHEMATICAL MODELING OF BIOLOGICAL SYSTEM

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**Abstract:** The computable aspect of the physical world's reality can be expressed using mathematics, which is a powerful instrument. As biological systems develop and adapt to their environment, mathematical relations internalise themselves as an abstracting capability. Internal coding structures that represent their embedded description are found in all living systems. They are anticipatory in the sense that a deterministic model of their behaviour is created by the embedded description. If the model doesn't yield the desired outcome, they can develop by acquiring additional statements within the embedded description that get around the shortcomings of the current model. The freshly generated assertions gain significance as a result of and because of the environment's change.

To better understand the biomedical data generated by high-throughput genomics and proteomics programmes, mathematical and computational models are being used more frequently. The use of sophisticated computer models that simulate complicated biological processes leads to the generation of hypotheses and recommendations for studies. properly integrating.

Models are required for quick access to, and sharing of knowledge using data mining and knowledge discovery techniques when faced with biological databases.

**Keywords :**Mathematical Biology ,Computational Model ,Biological Code ,Relation Biology.

## **Introduction:**

The computable aspect of the physical world's reality can be expressed effectively through mathematics. In the course of growth and adaptation to the outside world, mathematical relations occur internally in living systems as an abstracting capability. All living things have internal coding structures that serve as a representation of their embedded description. Insofar as the inherent description creates a deterministic model of their behavior, they are anticipatory. If the model does not yield the intended outcome, they can develop by acquiring fresh assertions within the embedded description that do away with the shortcomings of the prior model. As the environment changes, the freshly created statements change in meaning as well. A rapidly expanding body of biomedical knowledge is supported by numerous data sources, but our capacity for data analysis and interpretation is far behind that of data collection and storage.

Increasingly, high-throughput genomics and proteomics projects provide biomedical data that must be interpreted using mathematical and computational models. When complicated biological processes are simulated using cutting-edge computer models, hypotheses are generated and investigations. Through text mining and knowledge discovery techniques, computational models are prepared to take advantage of the vast amount of data available in biomedical databases.

Modeling is the practise of representing, modifying, and communicating everyday objects from real life. There are numerous ways to witness an item, or, equivalently, there are numerous different observers for the same object, as is readily apparent. There is no omniscient observer with exclusive access to the truth; instead, every observer has "various views" of the same object. Each individual observer gathers information and develops hypotheses that are in line with the information. This logical procedure is referred to as "abduction." Though we are all oblivious to a scientific mystery, abduction is not faultless.

A model is a description of a system's constituent elements and the relationships between them that can be encoded or understood by humans.

In general, a system is a mysterious "black box" (S) that, in response to a certain external stimulus (E), generates an output (R)

According to this broad definition, there are three main applications for models in science :

- (i) I synthesis or knowledge discovery: using knowledge of inputs E and outputs R to infer system characteristics;
- (ii) (ii) analysis and prediction: using knowledge of the components and their stimuli to explain for the observed response (i.e., output R) finally forecast response to various stimuli.
- (iii) Using an instrument or device, create a "alternative system" (i.e., hardware or software) that can closely resemble the system being studied while still reproducing the input-output relationship.

Secondary uses of models include conceptual frameworks for designing new experiments, techniques for summarising or synthesising vast amounts of data, and instruments for figuring out how objects are related to one another.

In this article, we examine biological models and modelling procedures. We primarily concentrate on (i) Use of models as methods for biology knowledge discovery that are aimed

(ii).Biological discovering tool.

The mathematical approaches used to represent biological systems change depending on the stage of the process. We concentrate on the system's mathematical representation. The fitting of parameters and the choice of models, however, are additional crucial elements in the modelling procedures. We won't discuss the mathematical approaches in those two crucial areas because separate review publications are needed for them. While approaches for model selection mostly involve statistical techniques, methods for parameters fitting cover a wide range of mathematical optimization. Additionally, the models may need to undergo sensitivity analysis and phase-space analysis. Models for technical usage are formal models, but their construction is done in a very different way, thus we won't discuss them in this discussion. These models will be referred to as "Black Box Models" in the sections that follow (BBM). It is important to note that, as we shall discuss later, alternative systems can be viewed as components of a larger model to account for effects whose origin can be disregarded without impairing our knowledge of the entire phenomenon.

## **Model of System :**

All scientific models may not necessarily have to be described precisely, numerically, and quantitatively. As a matter of fact, there are four basic kinds of models: verbal, conceptual or diagrammatic, physical, and formal.

### **Verbal Model:**

These models, which are based on observations, typically evidence the items and relations among the objects in the system in a straightforward manner. A verbal model is a crude and perhaps unclear qualitative representation of the system's knowledge. These models are employed in the initial method of biological system analysis.

## Diagrammatical Model:

In diagrammatic models, the objects are depicted graphically to describe the system.

in addition to the connections characterising the underlying dynamical processes. The grasp of the given data must be adequate to have a deep (though not exhaustive) understanding of the objects (or entities) and relations in order to create these types of models. A conceptual model (CM) depicts "concepts" (i.e., things or entities) and the connections among them. CM are often referred to as domain models in computer science. A CM is explicitly free of the design and is not constrained by implementation issues.

The purpose of a CM is to explain the meaning of words and concepts used by "domain experts" to rationalise the issue and identify connections between various concepts. To reduce issues brought on by varying understandings of terminology and concepts, the CM seeks to make clear the meaning of the frequently unclear phrases. The definitions of the various terms used should be connected to an existing "domain ontology" if one exists. The model becomes a solid foundation for the subsequent development of applications in that particular domain once the domain concepts have been modeled. Furthermore, manual or automated approaches to code generation can be used to map the conceptual model's ideas to actual physical design or implementation constructs.

## Physical Model:

In physical models, a mock-up of a real system or object is used to depict the subject (for example, a scale model of an aeroplane or ship). Engineers are especially interested in these types of models. They are frequently used to create smaller-scale prototypes when a system's properties are almost "scale-invariant," or unaffected by the size of the physical model created to represent the real system.

## Formal Model:

Formal models use mathematical frameworks to represent the system's knowledge. The mathematical representation of the model depends on the understanding of the system, some modelling decisions (such as the representation's spatial scale), and the modelling process's intended outcome. There are many different mathematical and computational approaches that can be applied, and choosing the right one often requires following rules that are dependent on experience. When choosing the best mathematical or computational method, there aren't many questions that come to mind. The system's description in terms of its various pieces or components, physical variables such as space and time, the kinds of relationships between things, and other issues are generally the focus of those problems. According to systems biology, a system is made up of various organs or compartments with various roles. 'Compartment models' are frequently employed in this situation, and each compartment may select a distinct mathematical representation.

Physical variables can be portrayed in models in a variety of ways. Additionally, the model may or may not take into account how the system has changed over time (dynamic versus static models). In terms of time-continuous versus time-discrete models, time can be viewed as either a continuous or discrete variable.

Similarly, the spatial distribution of objects in each compartment may or may not be relevant (heterogeneous versus homogeneous models). Finally, related things can be handled individually or in masse (particle models versus population models). Individual objects are identified in the first case by a unique state or by a large but finite set of states (one-state particle versus finite-state automata). Finally, object relationships can be described as deterministic or stochastic rules (deterministic versus stochastic models).

Single versus multicompartment models, including transport, evolutionary differential equations versus algebraic equations or spatial partial differential equations, differential equations versus difference equations, ordinary differential equations versus partial differential equations, kinetic methods, agent-based methods or cellular automata versus ODE or PDE; (stochastic ODE and PDE).

## Statistical and Artificial Based Model:

A statistical model is a formalisation of the relationships between variables in the form of mathematical equations; the only distinction between a statistical model and the mathematical models previously mentioned is the presence of uncertainty in each variable and/or parameter. One can use probabilistic measures and statistical or artificial intelligence methods to mimic the response relationship when the relationship between two things is too complicated to be reliably guessed. Because the model's goal is to accurately mimic the system's stimulus/response relation, a full investigation of the system components is typically omitted in models of this type. The lumped models with analogous circuits, neural networks,

## Modeling Process:

The steps involved in modelling are as follows:

- (i) Implementing the model entails using a mathematical structure or computer code to describe the objects and relationships found in the system under study,
- (ii) using the model to predict the behaviour of the system
- (iii) assessing the model's realism by comparing predictions with available data.

Finding a good model is difficult. Failure in modelling is not uncommon and it is a challenging topic in and of itself. A semi-formal set of rules is followed by the modelling procedure, which is a process in and of itself. The process is based on four large steps.

- (i) Create a plan for addressing the problem, i.e., specify a series of actions to be taken in order to find an appropriate model of the system under investigation,
- (ii) understanding the problem, which entails explicitly defining the questions one poses to the model, and doing so.
- (iii) Execute the plan, that is, carry out steps (ii) and (iv), assess the accuracy of the solution, and eventually improve the model.
- (iv) This final element is a crucial test to see whether the theory put out when creating the model is correct.

We are primarily interested in models for analysis and forecasting, as was previously noted. Figure 1 depicts the traditional description of the modelling procedure for these models. It is important to note that the schema shown in Figure 1 is not necessarily the most general one; rather, it is a general approach that may be used to models for analysis and prediction.

## Model Objective:

As we've already mentioned, defining the model objectives correctly is an important first step because it shows that the challenge has been understood to some extent. The purpose for creating a model should be obvious, and the objective should be properly defined to address the following issues:

- I. What is the system that has to be modelled
- II. What are the key questions that the model will address?
- III. How good the model must be and against what it will be measured
- IV. How will we interpret and apply the model's output?

Before we move further with our search for current knowledge about the system we desire to model, all of these questions must be answered because some information may be more pertinent than others.

## Current Knowledge:

Gathering information on the system being studied is an essential second phase in the modelling process. The scientific literature, including experimental findings, is consulted in this process, and it may also involve talking to subject-matter experts. The process of viewing the huge amount of information that is currently available can be greatly facilitated in the biomedical sector by data sets of literature record (such as Pubmed). Methods like data mining and data extraction may be quite helpful in this regard.

## **Model Structure:**

An actual system is represented by a model, which has its own structure. The model structure should be manageable and only include the knowledge that is thought to be pertinent to the study's goals (realism); the model results' level of detail should also be predetermined (precision); and finally, a model can be general, applicable to other systems like the one of interest, or specific to the system of interest (generality). Three qualities are in conflict: realism, precision, and generality. Each of these attributes compromises the other two. Finding a suitable balance between those conflicting features that satisfy the model aims is the process of choosing a model structure. Making a choice about the model structure is essential for formulating the model hypothesis, building diagrammatic models, and developing mathematical formulations.

## **Hypotheses:**

The next stage of the modelling process involves turning the goals and knowledge we want to incorporate into the model into a set of precise working hypotheses. Although they could also represent mathematical relationships, these are often verbal expressions. Working hypotheses are the cornerstone on which we will build our model, and they will determine how the model performs. It is important to evaluate the initial hypothesis when doing the model cycle refinement thoroughly and repeatedly.

## **Conceptual Model:**

The relevant system knowledge and model objectives that have been specified in the hypotheses are depicted graphically in the conceptual model. Objects and relations will be represented in a diagram in the conceptual model compartments where the collection of objects is fully defined and the relations are constrained.

## **Mathematical Formulation:**

The choosing of a mathematical structure that is acceptable for the model aims and capable of describing the hypotheses in quantitative form is usually the most challenging step in the modelling process. This process phase necessitates a certain amount of mathematical competence and, more importantly, calls for the definition of hazy notions and loose relationships in exact mathematical terms. A full description of the biological system can be useless if it is not required by the model objectives, thus it is clear that they are crucial. A formal model can be obtained by mapping a model into the mathematical domain using a mathematical formulation. Realisticism, Precision, and Generality are three qualities that must be balanced in a successful formal model, and it should also account for certain mathematical domain-specificity. In light of this, we can list the following as the main characteristics of formal models: Understandability: Providing a conceptual framework for considering the scientific domain; Compatibility: Transferring model hypothesis into a mathematical or computational infrastructure that can be solved to give the desired results with the required precision; Extensibility: Permitting the inclusion of additional real-world objects in the same mathematical scheme

Given the complexity of biology, a very detailed model of a biological system may prove to be computationally infeasible (for example, requiring the solution of too many equations or requiring the estimation of too many unknown parameters); in contrast, a model that is overly simplistic may not be able to take into account the complexity of the relevant biological system.

Domain specialists must be able to comprehend a formal model for it to be useful for their own quantitative reasoning. Finally, since biology is a rapidly expanding field of study, extensibility is a crucial quality for biological models. It should be simple to expand the model with modest changes to the mathematical framework when new objects and relations in the system are produced through laboratory tests.

## **Mathematical Formulation to Numerical Solution :**

Analytical analysis can only be performed on relatively simple models (i.e. by algebraic derivation of the system properties). The model is typically either directly implemented as computer code (i.e., the algorithm-like in ABM) or requires numerical equation solution. Even if there are many ways to solve equations, converting them into computer code is a potential source of error, so the best way to prevent mistakes caused by numerical instabilities must be carefully selected. Models of biological systems can have thousands of parameters and



dozens of dynamic variables, particularly when studying spatial processes. In this sense, comparing the computer results to the data that is provided is not a very difficult task.

### **Model Validation and Cyclic Refinement:**

The final step in the modelling process is the comparison of simulation results with model results. A model's main objectives are to recreate data from experiments or observations (descriptive models) or to forecast the outcome of future observations or experiments (predictive models). Naturally, outcomes must be validated in light of the model's goals. A quantitative agreement is required in some circumstances, whereas in others a qualitative agreement between model outputs and experimental data is sufficient. It is standard practise for model validation to demand that the model findings be verified using several sets of data. In spite of modifications in the model-free parameters, model outputs that do not suit the experimental data set point to the need for further model improvement. In this regard, one can find intriguing properties of the system of interest by going back and forth between model refinement and data validation. The activity itself results in the discovery of new information.

### **Model in Biology (Scale and complexity):**

Any natural phenomenon can be observed at several scales, as was already mentioned. As a result, while describing the phenomenon using conceptual and quantitative models, one must select the right size to account for the available experimental data.

However, there are features of practically all complex natural phenomena that cannot even be seen at a single scale of description (either temporal or spatial). Multi-scale models that depict things and connections on several levels of abstraction are necessary to examine these particular aspects of reality.

Choosing a scale relies on the characteristics of the phenomenon that one is interested in analysing, ranging from "micro" to "macro." This is a well-established strategy in physics that comes from several research fields, and it bases the distinction between scales on the typical lengths of objects and the typical duration of the events being studied. For instance, the field of physics known as "microphysics" studies phenomena that occur on the microscopic scale (length scales less than one millimetre), including: molecular physics, atomic physics, nuclear physics, and particle physics. The definition of a scale in the life sciences is a little less clear. The "cell" is a fundamental unit that can be used to define a scale, regardless of its physical dimension. Starting from here, one can define many scales, including the "sub-cellular," "intracellular," "cellular," "mesoscopic," and "intercellular scales." the "populations scale" and the "macroscopic scale."

Models created at the subcellular level deal with how a cell's physical and metabolic condition changes throughout time. This scale involves the nucleus and surface of the cell, as well as the genes, proteins, and signals that control cellular evolution and any signal processing activities that permit cell communication. As many biological specifics of a single cell's activity are unknown, modelling its overall activity is a particularly challenging challenge. In order to develop and apply mathematics and computer science tools in modelling sub-cellular processes, biologists and modellers have collaborated. The scientific literature is filled with references that interested readers can use. One is interested in describing the evolution of a system made up of numerous diversely interacting cells and molecules at the cellular level. Signals that cells send and receive through intricate recognition mechanisms control how cells interact with one another. Thus, there is a strong relationship between the cellular and subcellular scales. However, while modelling at this scale, one may forget the specifics of single cell models and treat them as BBM. This description uses mathematical techniques and tools from the fields of statistical mechanics, cellular automata, lattice gas, and other related disciplines.

The "macroscopic scale" includes tissues, organs (a group of tissues connected together structurally to fulfil a single function), systems (a collection of organs cooperating to complete a specific task), and organisms. The dynamical behaviour of observable quantities, often the concentrations of distinct things, is what is of interest at this scale (cells or molecules). Typically, methods derived from physical continuous systems, such as moments of kinetic equations or ordinary or partial differential equations, are used to model tissues. A model is necessary for defining organs in order to describe the primary tissue, sporadic tissues, and, most importantly, the biological function. One must take into account a network of organs that each carry out a distinct function while

modelling a system. The level of detail in a biological system model might vary depending on the objective of the model. Organs can be thoroughly described in terms of their individual parts or only as BBM carrying out a specific task. Connections between organs, such as lymphatic vessels, can be physically represented (by describing the fluid movements in the vessels dynamically) or simply by calculating the flux and the amount of time needed to transmit fluid from various organs, i.e. through the law of transport.

Finally, one is interested in explaining the dynamics of the populations in relation to one or more attributes at the population size. Models at this scale include those of epidemics or population controls. Because the influence of all the aforementioned scales and the environment on a single organism can change the population's overall dynamic, population dynamics is extremely complex. Depending on the scale of the populations that need to be described, a single organism in this class of models can or cannot be described in depth. Changes to an organism's primary characteristics must be taken into consideration in both scenarios. For instance, it is not necessary to describe in detail each single organism in order to understand how a community reacts to widespread vaccinations (as is necessary in influenza epidemics), but it may be necessary to take the population's age structure and environmental impacts into account. A sufficiently thorough description of each organism and the impact of the vaccination on each organism should be necessary when calculating the impact of a new vaccine for a small trial. For these classes of models, there are a number of different strategies available. In the first scenario, agent-based models (simple agents that represent a single organism) are used to explore the consequent complex phenomena, while ordinary or stochastic differential equations are used to describe the populations dynamics.

### **Complexity and Multiscale Model:**

Living things are intricate systems. A complex system is a system made up of various interrelated elements that, when taken as a whole, exhibit one or more features that do not naturally result from the characteristics of the individual parts, according to the "classical" definition. There are two types of system complexity: ordered complexity and unstructured complexity. While complexity in the former example results from a very large number of pieces, complexity in the latter situation is a natural property of the system, eventually with a small number of elements, and its linkages govern.

In living things, both circumstances exist. A living thing is made up of a variety of parts, each of which is an ordered complicated system. The human body's cells, organs, and systems are all extremely complicated.

As an illustration, the immune system, which is among the most complex, is made up of many parts (organs), constituents (cells and molecules), and regulations that connect scales of the parts in a hierarchical manner.

Both knowledge development and drug discovery now need models with multiple scales of a phenomenon. In the field of life sciences, both the whole live organism and its individual components are too complicated to be represented by a single, accurate, multiscale model. There is no doubt that the resulting model cannot be computed.

As a result, one is compelled to divide the conceptual model into a number of models that each describe a different aspect of the event (such as a single organ or a certain scale) and connect their results. It is difficult to connect models at various scales. Distinct scale phenomena typically have different characteristic time scales, therefore model output needs to be adequately matched. Another study in this issue is recommended to readers who are interested.

### **Tools And Applications:**

Biological systems are characterised by change and adaptation, whether we study the expansion and interactions of an entire population, the evolution of DNA sequences, the inheritance of features, the spread of disease, or the immune system's reaction to a virus. Even when they seem steady and stable, it is frequently the outcome of a balance of tendencies pulling the systems in various ways. The mathematical approach that is chosen depends on the biological system that you want to simulate. In this section, we outline a number of mathematical applications that have been successful in both replicating and offering fresh perspectives on a particular biological issue. Models that cover an entire biological system are currently rare and in fact incomplete due to

their tremendous complexity. Instead, a number of mathematical models that influence a single or group of biological system components are available.

## **Applications.**

### **Immunology:**

One of the most intricate areas of biology, immunology, has long been a subject of mathematical modelling. This recognition dates back to the 1960s and 1970s. Since then, various areas of immunology have used mathematical models. The testing of the pertinent biological variables when each experiment lasts less than a year is one of the main problems in the study on vaccines and other immunologic techniques. Scheduling extended immunizations is a prime illustration. The number of vaccination administrations should be as few as feasible to lower the chance of adverse reactions in humans, for example. In particular, the intensity of early immunizations was a crucial indicator of long-term tumour prevention needed for predictive value in the model, even though vaccination rates may be decreased without reducing efficacy. Long-term studies further supported *in silico* modeling's predictions that, if attained, an immunological plateau phase could be maintained with fewer vaccinations, demonstrating the importance of accurate mathematical modelling of early immune responses. This crucial illustration demonstrates how a combined *in vivo-in silico* strategy could enhance mathematical and biological models of cancer immunoprevention. The mathematical modelling of the mammary carcinoma-immune system competition provoked by an external stimulus is described by the authors [2] as an example of both qualitative investigation of the asymptotic behaviour and numerical simulations using nonlinear ODEs. A mathematical model created using the kinetic theory of active particles reported in a prior study [1] has been used to provide a model for keloid formation caused by virus, their malignant consequences, and immune system competition.

### **Circulatory System:**

The circulatory system is a biological system made up of organs that transports nutrients and other substances to and from body cells in order to fight disease, maintain homeostasis, and regulate body temperature and pH. Cardiovascular disorders, which are diseases related to this system, are very prevalent in Western nations. It has been shown that numerical simulations and mathematical models of the cardiovascular system can be used to better understand both its dynamics and potential treatments. A general overview of the mathematical representation of vascular geometries extracted from medical images, the modelling of blood rheology, the intricate multilayer structure of the vascular tissue, and its potential pathologies, as well as the mechanical and chemical interaction between blood and vascular walls, are all provided by the authors in a previous study [10].

### **Population Dynamics:**

The authors of a different study [8] describe and examine a periodically forced difference equation model for malaria in mosquitoes that takes into account the effects of seasonality and permits the mosquitoes to feed on a diverse population of hosts. Comparing the effectiveness of insecticide-treated nets (ITNs) and indoor residual spraying (IRS) in lowering malaria transmission, prevalence, and incidence, they integrate the difference equation model with an individual-based stochastic simulation model for human malaria. In addition to demonstrating that the combination of both interventions is more beneficial than either intervention alone, they also demonstrate that ITNs are more effective than IRS in reducing transmission and prevalence.

### **Drug Efficacy:**

The area of biology known as molecular biology is concerned with the molecular underpinnings of biological activity. Genetics and biochemistry are two fields of biology and chemistry with which this field has knowledge in common. Understanding the relationships between the many systems of a cell, such as those between various forms of DNA, RNA, and protein production, is possible thanks to molecular biology.

For a better understanding of disease causes and therapies, it is crucial to know how medications and diseases interact at the molecular level. Recently, in a paper the authors developed a Bayesian partition approach to find drug-gene-illness co-modules that underlie the gene closeness data. This method defines a network-based gene closeness profile to tie drug to disease. Their mathematical strategy and the associated simulations are applied



to a set of 1442 genes, 723 medicines, and 275 illnesses. It highlighted their biological basis and found new drug-disease correlations.

The study of tiny creatures, such as bacteria, viruses, fungus, prions, protists, and prokaryotes, is known as microbiology. This type of biological systems have received a tremendous amount of support from mathematical modelling, particularly in the study of the dynamics of pathogens. For instance, in ref. [24], the authors characterise the in vitro kinetic characteristics of the H5N1 avian, H1N1 seasonal, and H1N1 2009 pandemic influenza virus strains using differential equations and computer models. For the purpose of identifying and phenotyping possible pandemic strains, the technique offers pertinent parameters.

## Conclusion:

The higher levels of complexity in biological systems result from group behaviour and developing features at several levels. To begin with, this calls for the processing of significant amounts of low level data that have been obtained either directly through measurements or by accessing a number of sources. Then, these data must be incorporated into other multiscale or network models. A key stage in scientific discovery is the use of models. In this article, we discussed various model types that have been employed in biology for inference and knowledge discovery. Making a good model, however, is a difficult undertaking. We thoroughly examined the state-of-the-art in modelling to aid curious readers. Additionally, examples of current models and applications at various scales are shown in the final section of article.

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