Modeling a capital approach to biological risk assessment: An updated overview of the entropic scenario and the outcome of the upcoming microbial and ecological crises

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Abstract

Through this review paper we have presented the different applications of computational biology in three different research areas, microbiology, pharmacology and epidemiology.

The use of predictive models in bacteriology is simpler because the variables are well determined and the phenome is almost constant as well as the controlling factors.

In pharmacology the modeling takes two approaches, a linear one and a non-linear one, the difference is only significant between the definitive and continuous chemical reactions.

Modeling in epidemiology remains a challenge for the researcher in the field because the prediction depends on several parameters, ranging from the causative pathogen and its characteristics to the aspects of the impacted population. This diversity creates a wide divergence in the outcomes, which is difficult to estimate and generalize.

Modeling is a very powerful tool to investigate biological systems, mainly its forecasting and prediction, which helps to overcome potential hazards and risks, in the light of the global warming period and other related environmental damages.

Modeling has demonstrated its importance in finding quick solutions in the shortest time possible and the Corona epidemic is the best proof of this.

Key words: Modeling, predictive, forcasting, computational biology.

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Introduction

Studies and transactions have different names, and the subject matter is presented and encompassed, but there is no difference because all types of studies and the treatment of hypotheses are subject to pure mathematics, and the treatment of them is numerically abstractive and doesn't contemplate any logical overlaps and explanations or take into account the specialization. **(Saaty, 2004 ; Mangal & Mangal, 2013)**

Perhaps the return to specialization will occur after the mathematical analysis at the stage of interpretations and response to hypotheses, and this is where the role of mathematics and its arbitrary operations resides, for once mathematical logic, especially statistical, has prevailed, we have given credibility to our study, which is dominated by the logical-mathematical approach. **(Kingsland, 1995)**

A model is a simplified construction of a reality aiming at reproducing in order to knowledge that is not easily accessible through observation or experimentation because it is masked by its complexity. **(Oliva, 2003; Moreno et *al*; 2008)**

The models of biological systems try to describe in detail the parameters of the biological systems whereas mathematical models and simulation models are interested in the description of a system in order to description of a system in order to make predictions. **(Wiechert, 2002; Deutsch & Dormann, 2005; Haefner, 2005)**

Through this research paper, we will review the mathematical vision of the researcher in biology and life science through the most important mathematical methods used in the field, which is the one most complex and widely used, namely the computational modeling of biological phenomena.

the modelling handles many objectives, from the simplest one which is to provide a descriptive equation of a phenomenon or its progression and influential factors as in predictive microbiology, also to identify the possible scenarios for the dynamics and kinetics of a molecule as in pharmacokinetics or toxicokinetics and it can go very further with the estimation by the simulation which is the application of the modeling process similar to the epidemiological models used in the control and monitoring of pandemic.

1. predictive microbiology

A mathematical model is a systematic attempt to translate the conceptual understanding of a real system into mathematical terms. It is therefore an interesting way of understanding a process

occurring in the system under consideration National Research Council. If the conceptualization is good, the model should reproduce the relevant phenomena, thus a mathematical model is a valuable tool to verify our understanding of how a system works, and the model is a simplified representation of reality, facilitating prediction or estimation and is expressed in mathematical language. **(Torres & Santos, 2015; Sheridan & Hennessy, 1984).**

For example, in microbiology, modelling consists of constructing a model to describe the evolution of a bacterial population, and then making predictions about this development under new environmental conditions. **(Ross & McMeekin, 1994; Valdramidis, 2016).**

The focus was on the exponential growth phase. In 1983, Roberts and Jarvis termed this approach "predictive microbiology." **(Perez-Rodriguez & Valero, 2013).**

The assumption behind predictive microbiology is that the evolution of a bacterial population under given environmental conditions is reproducible; Thus, by considering the environmental conditions as the constraints defining a field of study, it is possible to predict the response of microorganisms from past observations. **(Altermatt et al; 2015).**

Predictive microbiology is a tool combining microbiological, mathematical and statistical elements to develop models describing the growth or destruction of microbial populations under certain environmental conditions. **(Fakruddin et al; 2011; Whiting, 1995).**

The published models describing the growth of microorganisms are mostly empirical models, they are developed from observations of experimental facts and there are also so-called mechanistic models that are built from theories about the behaviour of theories about the behavior of microorganisms and are therefore intellectually more satisfactory **(Callon, 1995; Stavropoulou & Bezirtzoglou, 2019)**; these mechanistic models are based on biological phenomena and their phenomena and their understanding, and are sometimes called phenomenological models. **(Craver, 2006).**

In practice, the two conceptions in some of the studies of microorganism growth are intertwined, with models combining mechanistic concepts with empirical observations. In the same way, many models, originally conceived in a totally empirical way, can eventually find mechanistic justifications. (**Pluta et al ; 2011).**

Whatever the chosen approach, descriptive or mechanistic, the criterion of parsimony (minimum number of parameters), and the biological or graphical significance of the parameters must always be respected. This last condition allows the parameters to be given an initial estimate that is consistent with the biological reality in order to fit the model to experimental data. **(Thornley & France, 2007; Anderson, 2008).**

a. Mathematical expression of bacterial growth

After a more or less long latency phase (bacterial adaptation in the culture medium), the growth is exponential, and can be described by one of the two following parameters: the generation time (***g***) or the exponential growth rate (***μ***). **(Isabelle & Andre, 2006).**

(***g***) is the population splitting time, which is the time interval in hours.

(***h***) that elapses between two cell divisions.

The growth rate (***μ***), is defined as the specific growth rate in (h-1) the growth rate (***dX/dt***) related to the unit of biomass(***X***).

A simple relationship between growth rate and generation time can be defined:

$\mu = \ln 2 / g$

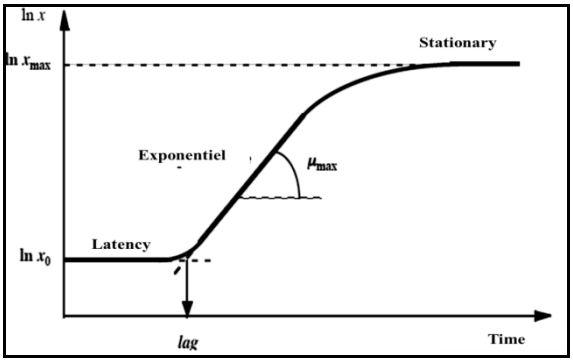


Figure 1. Growth curve (in semi-logarithmic coordinates) that better describes the growth parameters. (Peleg et al; 2007)

Main phases of the bacterial growth curve and parameters that characterize them; **lag** (lag time), μ_{max} (maximum growth rate), x_0 and x_{max} (initial and maximum cell densities).

The lag time ***lag***, is defined by convention as the intersection of the line corresponding to the exponential phase with the horizontal line passing through the initial concentration, x_0: The maximum multiplication rate or growth rate (growth rate per unit density), x_{max}: is the slope corresponding to the exponential phase (in semi-logarithmic coordinates).

The growth kinetics observed in practice are far from the simple and classical pattern shown in **Figure 1** and show a large variability. However, efforts have been made to model the first four or five phases of these kinetics.

The complexity of this biological phenomenon requires the use of nonlinear models to identify the growth parameters. The term parameter identification is understood here as the estimation of parameters by minimizing a convergence criterion. **(Chou et *al*; 2006).**

Bacterial growth kinetics are most often represented in semi-logarithmic coordinates, and the most obvious and classical method of estimating the maximum growth rate is therefore a linear regression analysis in the linear part of the curve corresponding to the exponential growth phase. **(Peleg, 2006).**

b. Classification of models.

Three classes of models have been proposed by Whiting and Buchanan (1993); primary, secondary and tertiary models.

Primary models describe the evolution over time of the microbial population in a specific environment. Depending on their complexity, they are characterized by one or more parameters such as lag time, growth rate, maximum density, etc...,

These parameters are specific to constant environmental conditions over time.

Models describing the effect of environmental conditions (pH, temperature, acids) on the parameters of the primary models are called secondary models.

The simplest model is the exponential model , which fits the exponential phase of growth well, but is poorly suited to describe the growths seen in nature, which are generally limited. **(Nielsen & Friberg, 2013).**

More complex models that generalize the exponential model by incorporating stationary growth phases and transitions between different growth phases have been proposed by many authors using the Gompertz model applied on the decimal logarithm of the bacterial concentration or the logistic model with delay and break. **(Zwietering et *al*, 1992).**

In 1985, a simple extension of the exponential model was proposed by Zamora and Zaritzky to take into account the lag phase; this model assumes that the start of exponential growth occurs abruptly without a transition phase and does not take into account either the saturation of the environment or the decay. **(Labuza et *al*, 1992).**

However, a simplification of these two models introduced the classical parameters: initial concentration (N_0), maximum concentration.

(N_{max}), lag time (***lag***) and growth rate (μ); they proposed the two models; Gompertz and the logistic model. Both assume that growth is maximal from the end of the lag time, which does not necessarily correspond to reality. **(Baty & Delignette-Muller, 2004).**

Baranyi et al. (1993) proposed a model combining the logistic braking function with kinetics of the transition of cells from the lag phase to the exponential phase.

Rosso (1995a) proposed the logistic model with breakthrough delay. It assumes the absence of growth during the lag phase and the transition between this phase and the exponential growth phase (break-up).

$dx/Xdt = \mu_{max}\ \alpha(t)\ f(x)$

$$f(x) = 1 - \frac{X}{Xmax} \qquad \& \qquad \alpha(t) = \frac{q(t)}{1+q(t)}$$

The function (t) is a strictly increasing sigmoid function, with values in [0,1] and tending towards 1 when t tends to infinity. The function $q(t)$ is the physiological state of the cell.

The integral form of this model is as follows:

$$y = y0 + A(t) - ln\left[1 + \frac{e^{\mu\, max\, A(t)} - 1}{e^{ymax - y0}}\right]$$ .....(Baranyi and Roberts, 1994)

This model is based on the assumption that adaptation occurs at the growth rate μ_{max} and therefore:

$\alpha(t) = \alpha(0) = e^{-h0}$ avec $h_{0} = ln[1 + 1/q_0]$

The Baranyi model is a four-parameter nonlinear model with: (**López et *al*, 2004)**

$y_0 = \ln(x_0)$ the neperian logarithm of the initial bacterial concentration,

$y_{max} = \ln(x_{max})$ the neperian logarithm of the maximum bacterial concentration that the starting population can reach, μ_{max} the maximum growth rate, h_0 a constant equal to the product of the growth rate and the *lag* time. **(Koutsoumanis et *al*, 2004).**

According to a more general version of the Baranyi model, the constant h_0 can be taken equal to $h_0 = \mu_{opt} \times lag_{min}$

The parameters μ_{op} and lag_{min} are the growth rate and lag time at the optimal growth temperature, respectively.

The Baranyi growth model is a primary model because it relates the bacterial population concentration to time; it belongs to the first level of modeling. The secondary models corresponding to the Baranyi model can be written as:

$$\boldsymbol{max} \text{ ou } \boldsymbol{h_0} \quad \boldsymbol{f(T, pH, aw; \theta)}$$

$\boldsymbol{T}$ and $\boldsymbol{pH}$ denote temperature and hydric potential, respectively, $\boldsymbol{a_w}$ is a variable correlated with the salt content of the culture medium. $\boldsymbol{\theta}$ is the parameter vector.

Models using expert and database systems to link the primary and secondary models are called tertiary models.

In parallel to this classification, dynamic models can be defined to predict microbial growth based on the parameters of the primary models that vary over time (time-varying environmental conditions).

The different types of equations used in predictive microbiology modeling are summarized in the following table.

Table 1. The different types of equations used in predictive microbiology modelling

Model		Equation
Primary $\ln(t)=f(t,\theta_1)+\varepsilon_\tau$	Exponential	$f(x)=\begin{cases} lnx0 & , t \le lag \\ lnx0+\mu\max\cdot(t-lag) & , t>lag \end{cases}$
	Logistic	$f(x)=lnx_0+\frac{A}{1+exp\left(\frac{4\cdot umax}{A}\cdot(lag-t)+2\right)}$
	logistic with lead times	$f(x)=\begin{cases} lnx0 & , t \le lag \\ lnx\max-\ln\left(1+(\frac{X\max}{X0}-1)\cdot\exp(-umax\cdot(t-lag))\right) & ,t>lag \end{cases}$
	Biryani	$f(t)=lnx_0+umax\cdot A(t)-ln\left(1+\frac{\exp(umax\cdot A(t))-1}{\frac{xmax}{x0}}\right)$ $A(t)=t+\frac{1}{\mu\max}\cdot ln[exp(-\mu\max\cdot t)+\exp(-\mu\max\cdot lag)-\exp(-\mu\max\cdot t-\mu$
	Gompertz	$f(x)=lnx_0+A\cdot exp\left[-exp\left(\frac{\mu\max\cdot e}{A}\cdot(lag-t)+1\right)\right]$
Secondary $\sqrt{umax}=a(e,\theta_2)+\varepsilon$	Square root	$g(T)=\begin{cases} 0 & ,T\le T\min \\ b\cdot(T-Tmin & ,T>T\min \end{cases}$

	Cardinals	$g(X) = \sqrt{u\,opt(X) \cdot CMn(X)}$ $CMn(X) =$ $\begin{cases} 0 & ,X \leq X\,min \\ \frac{(X-Xmax)\cdot(X-Xmin)^n}{(Xopt-Xmin)^{n-1}\cdot[(Xopt-Xmin)\cdot(X-Xopt)-(Xopt-Xmax)\cdot((n-1)Xopt+Xmin-n\cdot T)]} & \\ 0 & ,X \geq X\,max \end{cases}$ Xmax

2. Modeling in pharmacology & toxicology

The process by which we use mathematical expressions to describe a real quantitative situation is called modeling. Modeling consists of writing down in mathematical notation what is first expressed in words, involving variables as needed. **(Aris, 1994).**

In this case all the variables that are included in the model are independent of the individuals affected or exposed to the risk factors, the latter is purely anthropogenic, whereas the model obtained can be said to be an interaction model.

The linear model (fig. 2) is the most practical in this case and the formula used is :

$$\boldsymbol{y = f(X1, \ldots\ldots, X\rho; \alpha 0, \ldots\ldots, \alpha\rho)}$$

$$\boldsymbol{y = \alpha 0 + \sum_{j=1}^{\rho} Xj\alpha j + \varepsilon}$$

X_1,……,X_ρ **:** the studied variables.

$\boldsymbol{\alpha_0}$, $\boldsymbol{\alpha_1}$, …, $\boldsymbol{\alpha_p}$ **:** les parameters under study.

ε : the error of the model (uncertainty).

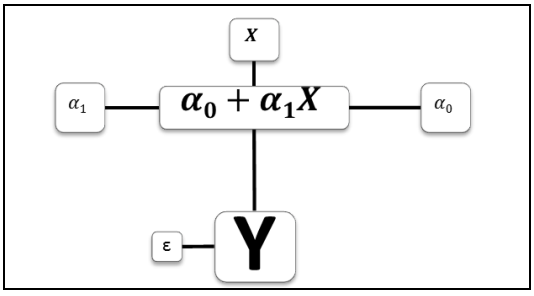


Fig 2. Linear mathematical model adequate for the modeling of xenobiotic dynamics.

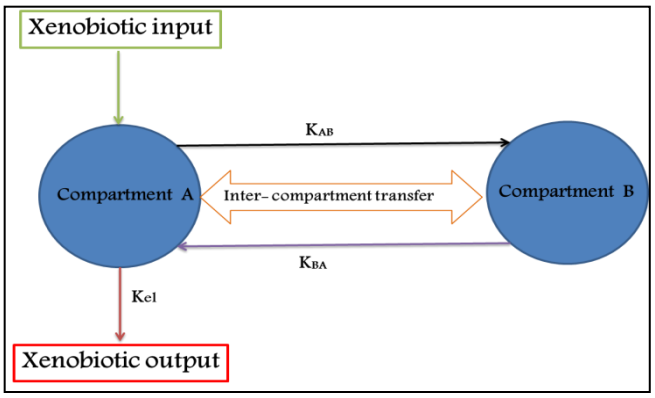


Fig 3. Symbolic pharmacological and toxicological model suitable for xenobiotic pathway modeling.

The model shown in Figure 3 can be described by the following system of ordinary differential equations:

$$\frac{dX(A)}{dt} = -[(K\,AB + Kel) \times X(A)] + KBA \times X(B)$$

$$\frac{dX(B)}{dt} = -KBA \times X(B) + KAB \times X(A)$$

With:

X(A) : amount of drug in compartment A

X(B) : amount of drug in compartment B

K_{AB} et K_{BA} : transfer constants between compartments A and B

K_{el} : elimination constant from compartment A

To these initial structural models, it is possible to graft specific compartments intended to represent certain particular structures of the organism, such as the organs in which the drug will diffuse and exert its action. These diffusion compartments then potentially have an anatomical reality. (Clairambault, 2009).

a. The PK/PD or TK/TD models

Generally when using an effective compound, one expects an enhanced action as the dose administered increases, in the case of an effect of the compound on the organism, or on the whole system, the dose administered, in the case of a continuous effect, an increase in the effect is expected. Continuous effect. It is thus implicitly assumed that there is a relationship between the dose of drug administered (*D*) and the expected effect E. Thus, if we consider a system having as

input the drug dose and as output an effect *E*, an effect model can be proposed, directly relating the administered drug dose *D* to the effect. **(Hayes & Loomis, 1996).**

$$E = f(\theta, D)$$

Represents the set of model parameters for example of a simple linear simple two-parameter model is the logarithmic model:

$$E = a.\ ln\ (D) + b$$

There are three major limitations to this kind of modeling, failure to account for inter-individual variability, absence of chronological dimension of the response and maximizing effect. **(Denechaud., 2020).**

b. Linear or log-linear models

Based on the principle of the simple dose/effect model, linear or log linear models linking the effects to the drug concentration have been proposed **(Holford & Sheiner, 1981).**

Their mathematical description is presented below:

$E = E_0 \pm a.C_{(t)}$ or $E = E_0 \pm a^*.lnC_{(t)}$ **……Pharmacology**

E_0 corresponds to a basal state in the absence of medication

$$\frac{dC\ \text{int}}{dt} = \boldsymbol{Kout(Cext(t) - Cint(t))}\text{……Toxicology}$$

K_{int}**:** absorption rate **.**

K_{out}**:** elimination rate.

$(dC_{int})/dt$**:** Bioaccumulation.

$K_{out}(C_{ext}\ (t) - C_{int}\ (t))$**:** Kinetics of effects.

c. Non-linear models

From the receptor occupancy theory, which applies the laws of physical chemistry to the effect produced by a drug on cells, a mathematical formalization has been proposed.

These models involve the ligand concentration [A], the receptor density [Rt], ε the intrinsic activity of the ligand and Ka the association constant between drug and receptor **(Pivonka & Komarova, 2010)**

Response $= f\left[\frac{[A]\times\varepsilon[Rt]}{[A]+Ka}\right]$ ➔ $E = \frac{Emax.C}{EC50+C}$ ➔ $E = \frac{Emax.C\gamma}{EC50\gamma+C\gamma}$

With E_{max} designating the maximum effect, and EC_{50} corresponding to the concentration for which the observed effect is equal to half of the maximum effect. This is in fact a special case of the called Hill model, which includes an additional parameter, sigmoidity coefficient γ.

For the toxicodynamic model the equation of a survival probability:

$$S(t) = e^{-\int_0^t h(t)dt}$$

And the mortality risk calculated by the following equation:

$$h(t) = \begin{cases} b(C\text{int}(t) - NEC + d & si\ C\text{int}(t) > NEC \\ d & si\ C\text{int}(t) > NEC \end{cases}$$

NEC: (No effect concentration).

d: (Background mortality).

b: (Killing rate).

The modeling of the effects (therapeutic or toxic) of drugs could be proposed by cited equations.

The TD/TK or PD/PK models built rely largely on nonlinear functions to achieve a complete description of the relationships between administered doses and observed effects can be achieved. **(Derendorf *et al*, 2000).**

3. Spatial diffusion models of diseases

Infectious disease diffusion models, formerly a strictly theoretical tool, gained acceptance as a decision-making tool for pandemics.

The use of models began with AIDS in the 1980s and has progressively asserted itself as a decision-making tool for pandemics. Since then, modeling continues to be an active research topic by integrating new tools proposed for example the network approach.

Models in epidemiology are first distinguished according to their deterministic or stochastic character. **(Kuhl, 2021; Price-Smith, 2008).**

A deterministic model for a set of parameters will have a fixed behavior, which means that the result is the same each time the model is run. means that the result is the same each time the model is run. On the other hand, a stochastic model stochastic model includes the notion of randomness; use of probability laws, which can be done by the variance of the parameters or by selecting events by drawing random, numbers (Monte-Carlo random numbers). Each realization of the model will give a different result; A stochastic model is in general less simplifying and allows including a biological variability, but conversely, from a mathematical point of view, it is

more difficult to manage and its results are more complex to analyze. **(Santner *et al.*, 2003; Othmer *et al.*, 1988).**

A simulation is the application of the modelling process. It differs according to its purpose. There on the one hand, there is the simulation to predict a state or to estimate a value: this one starts from an initial state known and/or fixed initial state. And on the other hand, there is the simulation whose purpose is the study of systems which do not exist or are poorly known: here the initial state is necessarily unknown and it is a question of determine which states are attainable from the possible initial states. The objective in this second case is to the acquisition of knowledge about the modelled system. **(Kuipers, 1986).**

A model can then be evaluated by performing a sensitivity analysis. A sensitivity analysis consists in quantifying the influence of the variability of a model parameter on the result. **(Hamby, 1994).**

Compartmental models divide the study population into epidemiological classes or behaviors defined by a health state. Most of the time, the following states (mutually exclusive) are used: susceptible S (never exposed to the pathogen), exposed E (in latency phase), infectious I (in infectious stage), immune R (cured and protected naturally or induced by vaccination). The state of the population is then described by the number of individuals in each compartment and its dynamics corresponds to the flows between compartments (SEIR model) **fig. 4. (Sturniolo., 2021; Getz et al; 2018).**

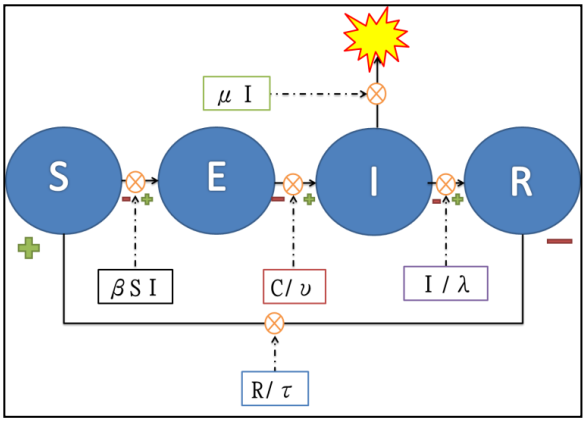


Fig 4. A model of an infection process in an epidemiological design.

The transition from the sensitive state to the exposed state is a stochastic event that occurs with occurs of the probability calculated at each time step.

An expression of this probability often encountered derives from a Poisson distribution and is written in its simplest form:

$P_E = 1\text{-}e^{-\beta\frac{1}{N}dt}$

P_E is the probability of an individual being infected between time t and $t + dt$, N is the total number of individuals in the study of individuals in the study population.

β is the transmission parameter. This rate takes into account the sensitivity and receptivity of individuals.

The strength of infection, noted **λ** (here, **λ =β I/N**) is the rate of susceptible individuals becoming infected in a heterogeneous population at a given time.

In many diseases, infectious agents return to the susceptible class upon recovery because the disease does not confer any immunity against reinfection. Such models are appropriate for most diseases transmitted by bacterial agents or helminths, and most sexually transmitted diseases (including gonorrhea, but not diseases such as AIDS) from which there is no recovery). We use the terminology SIS to describe a disease without immunity to reinfection, to indicate that the transition of individuals is from the susceptible class to the infectious class and back to the susceptible class classify. **(Meloni et al; 2011; Beldomenico & Begon, 2010).**

For example, the simple epidemiological model of Kermack-McKendrick One of the first triumphs of mathematical epidemiology was the formulation of a simple model by Kermack and McKendrick in 1927. this simple model whose predictions are very similar to the behavior , What has been observed in countless epidemics, which suddenly invade a population, increase in intensity, and then disappear leaving part of the population intact. **(Kermack & McKendrick, 1927).**

The Kermack-McKendrick model is a segmented model based on relatively simple assumptions about rates of movement between different population groups. Interest in epidemiological models, largely ignored since the days of Kermack and McKendrick, in favor of endemic models. **(Breda et al., 2012).**

$S' = -\beta SI$

$I' = \beta SI - \alpha I$

$R' = \alpha I.4764$

In this model, R is determined once S and I are known, and we can drop the R equation from this model, leaving the system of two equations:

$S = -\beta SI$

$I = \beta SI - \alpha I,$

Together with initial conditions $S(0) = S_0$, $I(0) = I_0$, $S_0 + I_0 = N$.

We introduced a small number of infected individuals to the group subject to disease and asked whether an epidemic would occur.

The model makes sense only as long as S(t) and I(t) remain nonnegative; if S(t) or I(t) reach zero, the system is considered finite. We note that $S < 0$ for any t and $I > 0$ only if and only if $S/\alpha > 1$. Thus I increases as long as $S/\alpha > 1$ but as S decreases for any t, I eventually decreases and approaches zero. The quantity $R_0 = \beta N/\alpha$ determines whether or not there is an epidemic. If $R_0 < 1$, the infection dies because $I(t) < 0$ by t, and there is no epidemic.

Typically, $S_0 \approx N$. If the epidemic was initiated by a member of the study population, such as returning from a trip with an infection contracted away from home, we would have $I_0 > 0$, $S_0 + I_0 = N$.

A second method would be the epidemic before a visitor from outside the population. In this case, we would have $S_0 = N$. If $R_0 > 1$, I will initially increase and this is interpreted as meaning that there is an epidemic. As a self-contained two-dimensional system of differential equations, the natural approach would be to find the equilibrium and linearity around each equilibrium to determine its stability. However, since every point with $I = 0$ is at equilibrium, the system has an equilibrium line and this approach is not applicable (the linearity matrix at each equilibrium has an eigenvalue of zero). The standard linear theory does not apply to systems of ordinary differential equations, and it is necessary to develop a new mathematical approach. The sum of the two equations is $(S + I) = -\alpha I$.

So S + I is a nonnegative smooth decreasing function and therefore tends to be bounded when $t \rightarrow \infty$. Moreover, it is not difficult to prove that the derivative of the smooth decreasing function defined below must tend to zero, which shows that $I\infty = \lim t \rightarrow \infty I(t) = 0$. So S + I has limit $S\infty$.

Integration of the sum of the two equations from 0 to ∞ gives

$$-\int_0^\infty S(t) + I(t))\, dt = S0 + I0 - S\infty = N - S\infty = \alpha \int_0^\infty I(t) dt.$$

Division of the first equation of S and integration from 0 to ∞ gives

$$\log \frac{S0}{S\infty} S_0\, S_\infty = \beta \int_0^\infty I(t) dt.$$

$$= \frac{\beta}{\alpha} [N - S_\infty]$$

$$= R_0 \left[1 - \frac{S\infty}{N}\right] \quad .4765$$

Equation is called the final size relation; it gives a relation between the basic reproduction number and the size of the epidemic. **(Andreasen, 2011)**

Note that the final size of the epidemic, the number of members of the population who are infected over the course of the epidemic, is $N - S_\infty$.

This is often described in terms of the attack rate ($1-S_\infty/N$). [Technically, the attack rate should be called an attack ratio, since it is dimensionless and is not a rate]. The attack rate is the fraction of the population that becomes infected over the course of the epidemic. The final size relation can be generalized to epidemic models with more complicated compartmental structure than the simple SIR model, including models with exposed periods, treatment models, and models including quarantine of suspected individuals and isolation of diagnosed infectives. **(Brauer *et al*; 2019)**

The original Kermack–McKendrick model included dependence on the time since becoming infected (age of infection), and this includes such models.

Integration of the first equation from 0 to t gives.

$\log S_0\, S(t) = \beta \int_0^t I\,(t)dt$

$= \frac{\beta}{\alpha}\,[N - S(t) - I(t)]$,

$I\,(t) + S(t) - \alpha / \beta \log S(t) = N - \alpha/\beta \log S_0$.

This implicit relation between S and I describes the orbits of solutions in the (S, I) plane. In addition, since the right side of equation is finite, the left side is also finite, and this shows that $S\infty > 0$.

It is not difficult to prove that there is a unique solution of the final size relation. To see this, we define the function4766.

$$\begin{cases} g(x) = log\frac{S0}{x} - R_0\,[1 - \frac{x}{N}] \\ g(0+) > 0, g(N) < 0\ and\ g'(x) < 0\ if\ and\ only\ if\ 0 < x < \frac{N}{R_0} \end{cases}$$

If $R_0 \leq 1$, $g(x)$ is monotone decreasing from a positive value at x = 0+ to a negative value at x = N. Th us there is a unique zero $S\infty$ of $g(x)$ with $S\infty < N$.

If $R_0 > 1$, $g(x)$ is monotone decreasing from a positive value at X = 0+ to a minimum at $x = N/R_0$ and then increases to a negative value at $X = N_0$. Th us there is a unique zero $S\infty$ of $g(x)$ with $S\infty < N/R_0$.

In fact, $g\left(\frac{S0}{R0}\right) = \log R_0 - R_0 + S_0/N$

$\leq \log R_0 - R_0 + 1$.

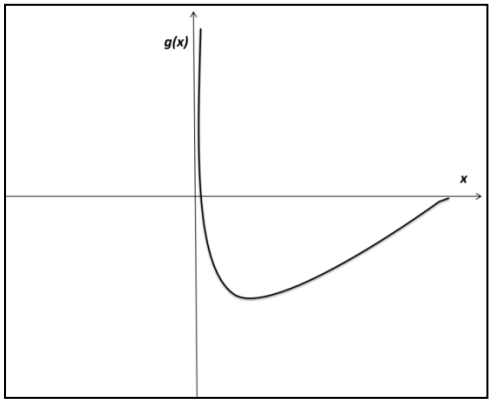
Since log $R_0 < R_0 - 1$ for R0 > 0 and $S\infty < S_0 / R_0$, we actually have

$$g\left(\frac{S0}{R0}\right) < 0 ,$$

An important question is how the basic reproduction number changes if a parameter of the model varies. If R_0, and therefore S∞, is a function of a parameter η, implicit differentiation of the final size relation gives $(R_0 /N - 1/ S_\infty)\, dS_\infty / d\eta = d R_0 / d\eta\, (1 - S_\infty /N)$.

Because of if R_0 increases then S∞ decreases.

A graph of the function *g(x)* presented in **figure 5**.



The finals formule of the model are

$$p > 1 - \alpha / \beta N = 1 - 1/ R_0 .$$

Initially, the number of infectives grows exponentially because the equation for I may be approximated by :

$$I = (\beta N - \alpha) I$$

$$r = \beta N - \alpha = \alpha (R_0 - 1)$$ 4767

Simple Compartmental Models for Disease Transmission This initial growth rate r may be estimated from incidence data when an epidemic begins. Since N and α may be measured, β may be calculated as:

$$\beta = r + \alpha/N.$$

However, because of incomplete data and under-reporting of cases, this estimate may not be very accurate. This inaccuracy is even more pronounced for an outbreak of a previously unknown disease, where early cases are likely to be mis-diagnosed. Because of the final size relation, estimation of β or R_0 is an important question that has been studied by a variety of approaches. Estimation of the initial growth rate from data can provide an estimate of the contact rate β.

However, this relation is valid only for the model and does not hold for models with different compartmental structure, such as an exposed period. **(Manski & Molinari, 2021).**

If $\beta S0 > \alpha$, I increases initially to a maximum number of infective when the derivative of I is zero, that is, when $S = \alpha/\beta$. This maximum is given by

$$\mathbf{I_{max} = S0 + I0 - \alpha/\beta \log S0 - \alpha/\beta + \alpha/\beta \log \alpha/\beta,}$$

Obtained by substituting $\mathbf{S = \alpha/\beta}$, $\mathbf{I = I_{max}}$ in the previous equation.

Conclusion

Computational analysis of natural data phenomena has undergone a considerable progress linked to artificial intelligence and computing machines, though the same was mainly based on mathematics and processed life in its quantum and data processing aspects.

Modeling is one of the most effective ways to study natural mechanisms, especially the forecasting and predicting ones, and provides a great hope to outperform the resulting dangers in the light of the period of Global Climate Warming and other major environmental damages. Modeling demonstrated its significance in finding quick solutions in the shortest possible time and Corona virus is the best evidence.

References

[1] Altermatt, F., Fronhofer, E. A., Garnier, A., Giometto, A., Hammes, F., Klecka, J., ... & Petchey, O. L. (2015). Big answers from small worlds: a user's guide for protist microcosms as a model system in ecology and evolution. *Methods in Ecology and Evolution*, *6*(2), 218-231.

[2] Anderson, D. R. (2008). Information theory and entropy. *Model based inference in the life sciences: A primer on evidence*, 51-82.

[3] Andreasen, V. (2011). The final size of an epidemic and its relation to the basic reproduction number. *Bulletin of mathematical biology*, *73*(10), 2305-2321.

[4] Aris, R. (1994). *Mathematical modelling techniques*. Courier Corporation.

[5] Baty, F., & Delignette-Muller, M. L. (2004). Estimating the bacterial lag time: which model, which precision?. *International journal of food microbiology*, *91*(3), 261-277.

[6] Beldomenico, P. M., & Begon, M. (2010). Disease spread, susceptibility and infection intensity: vicious circles?. *Trends in Ecology & Evolution*, *25*(1), 21-27.

[7] Brauer, F., Castillo-Chavez, C., & Feng, Z. (2019). *Mathematical models in epidemiology* (Vol. 32). New York: Springer.

[8] Breda, D., Diekmann, O., De Graaf, W. F., Pugliese, A., & Vermiglio, R. (2012). On the formulation of epidemic models (an appraisal of Kermack and McKendrick). *Journal of biological dynamics*, *6*(sup2), 103-117.

[9] Buchanan, R. L. (1993). Predictive food microbiology. *Trends in Food Science & Technology*, *4*(1), 6-11.

[10] Callon, M. (1995). Four models for the dynamics of science. In *Science and the Quest for Reality* (pp. 249-292). Palgrave Macmillan, London.

[11] Chou, I. C. H. M., Martens, H., & Voit, E. O. (2006). Parameter estimation in biochemical systems models with alternating regression. *Theoretical Biology and Medical Modelling*, *3*(1), 1-11.

[12] Clairambault, J. (2009). Modelling physiological and pharmacological control on cell proliferation to optimise cancer treatments. *Mathematical Modelling of Natural Phenomena*, *4*(3), 12-67.

[13] Craver, C. F. (2006). When mechanistic models explain. *Synthese*, *153*(3), 355-376.

[14] Denechaud, C., Smoliński, S., Geffen, A. J., Godiksen, J. A., & Campana, S. E. (2020). A century of fish growth in relation to climate change, population dynamics and exploitation. *Global Change Biology*, *26*(10), 5661-5678.

[15] Derendorf, H., Lesko, L. J., Chaikin, P., Colburn, W. A., Lee, P., Miller, R., ... & Venitz, J. (2000). Pharmacokinetic/pharmacodynamic modeling in drug research and development. *The Journal of Clinical Pharmacology*, *40*(12), 1399-1418.

[16] Deutsch, A., & Dormann, S. (2005). *Mathematical modeling of biological pattern formation* (pp. 45-56). Birkhäuser Boston.

[17] Fakruddin, M. D., Mazumder, R. M., & Mannan, K. S. B. (2011). Predictive microbiology: Modeling microbial responses in food. *Ceylon J. Sci*, *40*(2), 121-131.

[18] Getz, W. M., Salter, R., Muellerklein, O., Yoon, H. S., & Tallam, K. (2018). Modeling epidemics: A primer and Numerus Model Builder implementation. *Epidemics*, *25*, 9-19.

[19] Haefner, J. W. (2005). *Modeling biological systems:: principles and applications*. Springer Science & Business Media.

[20] Hamby, D. M. (1994). A review of techniques for parameter sensitivity analysis of environmental models. *Environmental monitoring and assessment*, *32*(2), 135-154.

[21] Hayes, A. W., & Loomis, T. A. (1996). *Loomis's essentials of toxicology*. Elsevier.

[22] Holford, N. H., & Sheiner, L. B. (1981). Understanding the dose-effect relationship. *Clinical pharmacokinetics*, *6*(6), 429-453.

[23] Isabelle, L., & Andre, L. (2006). Quantitative prediction of microbial behaviour during food processing using an integrated modelling approach: a review. *International Journal of Refrigeration*, *29*(6), 968-984.

[24] Kermack, W. O., & McKendrick, A. G. (1927). A contribution to the mathematical theory of epidemics. *Proceedings of the royal society of london. Series A, Containing papers of a mathematical and physical character*, *115*(772), 700-721.
[25] Kingsland, S. E. (1995). *Modeling nature*. University of Chicago Press.
[26] Koutsoumanis, K., Stamatiou, A., Skandamis, P., & Nychas, G. J. (2006). Development of a microbial model for the combined effect of temperature and pH on spoilage of ground meat, and validation of the model under dynamic temperature conditions. *Applied and Environmental Microbiology*, *72*(1), 124-134.
[27] Kuhl, E. (2021). *Computational Epidemiology*. Springer International Publishing.
[28] Kuipers, B. (1986). Qualitative simulation. *Artificial intelligence*, *29*(3), 289-338.
[29] Labuza, T. P., Fu, B., & Taoukis, P. S. (1992). Prediction for shelf life and safety of minimally processed CAP/MAP chilled foods: a review. *Journal of food protection*, *55*(9), 741-750.
[30] López, S., Prieto, M., Dijkstra, J., Dhanoa, M. S., & France, J. (2004). Statistical evaluation of mathematical models for microbial growth. *International journal of food microbiology*, *96*(3), 289-300.
[31] Mangal, S. K., & Mangal, S. (2013). *Research methodology in behavioural sciences*. PHI Learning Pvt. Ltd..
[32] Manski, C. F., & Molinari, F. (2021). Estimating the COVID-19 infection rate: Anatomy of an inference problem. *Journal of Econometrics*, *220*(1), 181-192.
[33] Meloni, S., Perra, N., Arenas, A., Gómez, S., Moreno, Y., & Vespignani, A. (2011). Modeling human mobility responses to the large-scale spreading of infectious diseases. *Scientific reports*, *1*(1), 1-7.
[34] Moreno, A., Etxeberria, A., & Umerez, J. (2008). The autonomy of biological individuals and artificial models. *BioSystems*, *91*(2), 309-319.
[35] Nielsen, E. I., & Friberg, L. E. (2013). Pharmacokinetic-pharmacodynamic modeling of antibacterial drugs. *Pharmacological reviews*, *65*(3), 1053-1090.
[36] Oliva, R. (2003). Model calibration as a testing strategy for system dynamics models. *European Journal of Operational Research*, *151*(3), 552-568.
[37] Othmer, H. G., Dunbar, S. R., & Alt, W. (1988). Models of dispersal in biological systems. *Journal of mathematical biology*, *26*(3), 263-298.
[38] Peleg, M. (2006). *Advanced quantitative microbiology for foods and biosystems: models for predicting growth and inactivation*. CRC Press.
[39] Peleg, M., Corradini, M. G., & Normand, M. D. (2007). The logistic (Verhulst) model for sigmoid microbial growth curves revisited. *Food research international*, *40*(7), 808-818.
[40] Perez-Rodriguez, F., & Valero, A. (2013). Predictive microbiology in foods. In *Predictive microbiology in foods* (pp. 1-10). Springer, New York, NY.

[41] Pivonka, P., & Komarova, S. V. (2010). Mathematical modeling in bone biology: From intracellular signaling to tissue mechanics. *Bone*, *47*(2), 181-189.
[42] Pluta, W. J., Chinn, C. A., & Duncan, R. G. (2011). Learners' epistemic criteria for good scientific models. *Journal of Research in Science Teaching*, *48*(5), 486-511.
[43] Price-Smith, A. T. (2008). *Contagion and chaos: disease, ecology, and national security in the era of globalization*. MIT press.
[44] Ross, T., & McMeekin, T. A. (1994). Predictive microbiology. *International journal of food microbiology*, *23*(3-4), 241-264.
[45] Saaty, T. L. (2004). *Mathematical methods of operations research*. Courier Corporation.
[46] Santner, T. J., Williams, B. J., Notz, W. I., & Williams, B. J. (2003). *The design and analysis of computer experiments* (Vol. 1). New York: Springer.
[47] Sheridan, T. B., & Hennessy, R. T. (1984). *Research and modeling of supervisory control behavior. Report of a workshop*. National Research Council Washington DC Committee on Human Factors.
[48] Stavropoulou, E., & Bezirtzoglou, E. (2019). Predictive modeling of microbial behavior in food. *Foods*, *8*(12), 654.
[49] Sturniolo, S., Waites, W., Colbourn, T., Manheim, D., & Panovska-Griffiths, J. (2021). Testing, tracing and isolation in compartmental models. *PLoS computational biology*, *17*(3), e1008633.
[50] Thornley, J. H., & France, J. (Eds.). (2007). *Mathematical models in agriculture: quantitative methods for the plant, animal and ecological sciences*. Cabi.
[51] Torres, N. V., & Santos, G. (2015). The (mathematical) modeling process in biosciences. *Frontiers in Genetics*, *6*, 354.
[52] Valdramidis, V. (2016). Predictive microbiology. In *Modeling in food microbiology* (pp. 1-15). Elsevier.
[53] Whiting, R. C. (1995). Microbial modeling in foods. *Critical Reviews in Food Science & Nutrition*, *35*(6), 467-494.
[54] Wiechert, W. (2002). Modeling and simulation: tools for metabolic engineering. *Journal of biotechnology*, *94*(1), 37-63.
[55] Zwietering, M. H., Jongenburger, I., Rombouts, F. M., & Van't Riet, K. J. A. E. M. (1990). Modeling of the bacterial growth curve. *Applied and environmental microbiology*, *56*(6), 1875-1881.
[56] Zwietering, M. H., Rombouts, F. M., & Riet, K. V. T. (1992). Comparison of definitions of the lag phase and the exponential phase in bacterial growth. *Journal of Applied Bacteriology*, *72*(2), 139-145.