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# Mathematical Modeling: Proposal of a General Methodology and Application of This Methodology to Epidemiology

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**Abstract:** We propose a general methodology allowing modeling the natural phenomena mathematically. After having to clarify the concepts and to propose a classification of the models according to their functions of description, prediction and comprehension, we give a definition of the mathematical model which integrates prediction and comprehension. Thereafter, we propose with details the great stages of mathematical modeling. An application of methodology suggested is made in a general way in epidemiology. Finally we proceed in example to the modeling and mathematical analyis of influenza epidemic in a heterogeneous environment taking account the mobility of the individuals.

**Keywords:** Modeling; Mathematical model; Dynamical system; Epidemiology.
**Mathematics Subject Classification (2010):** 92D30, 93A30, 74S20.

## 1. Introduction

The mathematical modeling which since very long years, has reached science as a whole, is not defined by covering of only one or some restricted sectors of science, nor by a quite identifiable object of study. This practice of which the essence consists in the replacement of the original object by its mathematical model [1] seem to profit from a ”low esteem” in the sense that each field of the science which it employment develops its own techniques, posing some times of the dissensions in the definition of the concept even of mathematical model.

For the engineers of the sixteenth century, the model had the double function to persuade and to allow simulation [2].

It is in fact the physics which will develop in an intensive way the practice of the models, at the end of the nineteenth century, before rather quickly inspiring biology in return. But this use of the concrete models in biology will be renewed in measurement even where physics, preceding biology, opened the knowledge with fields of phenomena, therefore with fields of analogies, new, of which more particularly that of electricity [3].

It should well be understood that, in physic of the nineteenth century, the main aim of modeling indeed was from the start to go accessible from the phenomena until there badly controlled because incompletely theorized. The principal stake of the models, in physics, is well, in this context, to increase a mathematical control. But this will of mathematical control is ambiguity and is not interpreted everywhere in the same manner : either it is thought that this will simply orders to go capable to build the adequate mathematical formalism, or it is considered that the detention of this formalism must double of a intellectual control of mathematics concerned, especially if it is new.

Indeed, it would be in front of the question of the transfer of heat that the modern practice of modeling would have furbished promising weapons and would have developed effectively, to the direction where it would have succeeded in introducing directly mathematical tools in a discipline hitherto rebel with the precise prediction because dedicated to ”qualities second”, according to the philosophical tradition. Method of mathematical models entered the life sciences initially in ecology, in dynamics of the populations, genetics and biometrics. At the beginning of twentieth century, ecologists were more related to work in field and laboratory. Less versed in mathematical formalization and very skeptics in his connection, they thus were initially outdistanced by researchers come from physical sciences and social sciences, like demography. In the years 1920, for number of ecologists and naturalists, it still did not seem possible to capture and make hold in equations the complexity of the real alive world. Models then had generally the form of differential equations or systems of differential equations. The variables represented respective manpower of the species or of age groups. However, in order to be able to use this type of models, the ecology of the populations made in effect several restrictive assumptions which could be used besides to draw the contour of it scientific discipline, before it comes, later, to interfere and merge with the genetics of the populations to form the dynamics of the populations: on the one hand, the populations were supposed not to vary genetically. In

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addition, the physical environment also was supposed to remain the same one. These models were thus, could one say, rather not very dynamic: they assigned of dynamics only to the variables considered to be interesting. Nevertheless, certain ecologists overcame their mistrust little by little first and they wanted to test these models in experiments. These first modelers in ecology of the populations had to learn how to integrate in a new way the approaches of ground, the experiments and the theoretical approaches. One can say thus that in the middle of the years 940, it existed already a ”alive community ecologists of the populations in ecology”.

In the years of post-war period, the ecology of the populations started to admit that it would not find laws simple of the type of those which one sees appearing in physics. The models then became more sophisticated, but especially the recourse to systematic data analysis is intensified and that thanks to the first developments of the computer. The game theory finally, as well as mathematical programming, borrowed for their part from the economy, seemed to be able to provide other mathematical formalisms to ecology. All these new styles available, as well as the development of the models of analysis of data, made blow a wind of freedom which announced an easing of the mathematical tool and thus its possible taking into account of the complexity of the alive one. In dynamics of the populations, the models became increasingly realistic and detailed then, their performances depending always more on those of the computers available. The research of increased predictive capacities was indeed supported by the social request, emanating itself from an awakening and an institutional taking into account general then of various ecological threats of scale.

It is at that time of strong expansion of the dynamics of the populations of the type immediately operational and pragmatic, could we say, that an approach alternative mathematics starts to take its rise. This scission between empirical and ideal model models in ecology joined a partition then of the same type, already with work since the years 1930, in economy.

This article is organized in the following way: with the section 2, we define the basic concepts in mathematical modeling and specify the types of models. In section 3 we give the great stages of mathematical modeling. After having to specify the role of the numerical simulations in mathematical modeling, an application of methodology given is made in epidemiology in section 5.

# 2. Model and Modeling

In the beginning, a model is an object intended to be imitated [4]. Thus, the model word highlights two things: the original and the imitation. In general, the original represents the real phenomenon and the model is rather the imitation obtained. Process which makes it possible to pass from the real phenomenon to the model is called modeling.

**Definition 2.1.** Mathematical modeling is the partial or total imitation of a real phenomenon by one or more mathematical theories.
**Definition 2.2.** A mathematical model is the representation in mathematical terms of a real phenomenon.
**Remark 2.3.** The model is an imitation, it is thus essentially false. One must think of modeling that only if it real phenomenon cannot directly be to apprehend effectively in its ”natural environment”.

## 2.1. Types Of Models: To Describe, Predict Or Understand?

The models are generally classified in three great groups according to their function: descriptive models, predictive models and scientific models.

### 2.1.1. Descriptive models

They are the static models which consist with a diagrammatic representation (sketch) of the real phenomenon. Such models are not dynamics and do not allow to conduct forecasts or to understand the mechanisms of operation of the real phenomenon.

## 2.1.2. Predictive Models

Still called statistical models, they act of the models frames starting from the data resulting from the real phenomenon. Such a model is a relation (between variables) expressible in an analytical or algorithmic form which does not come from a theory but is resulting from the exploration of the data and carries out a good adjustment. These models are of a pragmatic optics: it is not a question inevitably to understand but predict as well as possible.

The strong point of the statistical models is related to be able to them of inference conferred by the tests of assumptions. These tests of assumptions are powerful as soon as one is located within a quite rigorous framework.

The weak point of the statistical models is related to this framework which imposes relations between extremely simple variables (often linear). These relations are primarily descriptive and do not allow to in no case to reach a mechanistic comprehension of the system (i.e to know how the system functions).

## 2.1.3. Scientific Models

There exist situations where one does not have any data on the real phenomenon. In this case to build the model one is limited to a pure reasoning. For such situations, scientific theories in particular mathematics seem one invaluable tool insofar as they constitute a language allowing to reason in the most concise way, more rigorous and most effective possible. The models thus obtained are called scientific models.

The strong point of the scientific models is that they make it possible to in depth clarify the mechanisms of operation of the real phenomenon and by there, to identify the key elements.

The weak point of these models is their absence of bond with any form of real data, often conferring a strictly speculative value to them.

It is a very fertile field of research today which to try to combine the advantages of the statistical models (inference) and scientific models (mechanisms).

**Definition 2.4.** The *mathematical models* are scientific models which make it possible to fill the lacks of observations and tending towards a total comprehension of the real phenomenon, in spite of partial data. They make it possible to predict and understand the real phenomenon.

## 2.2. Deterministic, Stochastic and Fuzzy Models

### 2.2.1. Deterministic Models

The determinism rests at the same time on a natural objective order, causality, because it supposes that all that occurs is the effect of determined causes, and on a subjective order, the prediction, which supposes the exact forecast of effects produced starting from the conditions given. [5].

A model is known as deterministic when the variables (of states) described by this model are the effect of causes clearly determined, and so starting from the conditions given, it makes it possible to carry out predictions with hundred percent.

**Remark 2.5.** By causes clearly determined, we understand causes necessary to explain the real phenomenon.

### 2.2.2. Stochastic Models

The indeterminism is based on a random interpretation (i.e hazardous) of the physical phenomena, the word hazard having three different acceptances [5]:

From an epistemological point of view, the hazard is what is spontaneous and unspecified (under identical conditions, a system will evolve sometimes in a direction, sometimes in another).

From a point of view of foreseeability, the hazard is what is unforeseen, unexpected and unforeseeable (the hazard is the expression of my ignorance, an effect not envisaged, a non desired action).

Lastly, from the teleological point of view, the hazard is the astonishment which expresses a causal sequence (a disproportion of the effect compared to the cause, a succession of events which deviates from the usual frequency) and becomes a business of long-term regularity (laws of fate, laws of the great numbers, etc.).

A model is known as stochastic when the variables (of states) described by this model are the effect of unspecified causes.

### 2.2.3. Fuzzy Models

Incompleteness is one facet of uncertainty and randomness is the other, and when there does not exist enough of available data to develop the probability distributions of certain parameters, it becomes imperative then to use fuzzy set theory to model the uncertainty.

A model is known as fuzzy when the variables (of states) described by this model are regarded as nonrandom and vague.

# 3. Great Stages of Mathematical Modeling

## 3.1. Identification of the Profile

The first stage in the mathematical modeling of a real phenomenon consists in identifying clearly and with the absolute precision what one wishes to imitate of the real phenomenon: us let us call *the profile*.

The formulation of this profile makes it possible to release the first assumptions of modeling which are summarized with the physical description of the profile. On this level, additional assumptions can also be formulated with the aim of implement the mathematical theories effectively having to lead to the model.

## 3.2. Identification of the Dynamism of the Profile

Once identified profile, it is necessary to have information on its dynamism, i.e to know if this profile is a phenomenon which varies in time (evolutionary phenomenon) or if it is rather about a static profile (non evolutionary phenomenon).

If the profile is dynamic then the discounted model is a dynamical system (T, X, A, S) where X represents the space of state, T the space of time, A the set of the initial conditions and S a family of movements [6].

If the profile is static then the discounted model is described by explicit mathematical relations independent of times connecting the key variables of the profile. *N.B. The stages which follow relate to the case of a dynamic profile.*

## 3.3. Description of Space Time and the Space of State

When the profile is dynamic then the discounted model is a dynamical system (T, X, A, S). It is thus necessary in this case clearly to clarify spaces T and X.

### 3.3.1. Choice of Space Time

The mathematical models are scientific models consequently, space time to choose must be that in which the profile takes place and not that in which the data are collected. Thus if the profile takes place in real-time (i.e in a permanent way without interruption), one will take $\subseteq \mathbb{R}^+$ : it is the *continuous time*. So on the other hand the profile takes place in isolated times (i.e with interruptions), one will take $T \subseteq \mathbb{N}$: it is the *discrete time*.

### 3.3.2. Choice of the Space of State

The space of state is the physical space (environment) in which the profile takes place. If this space consists of isolated points (i.e profile unrolls in a countable number of points) one will take $\subseteq \mathbb{Z}^n$ $(n \in \mathbb{N}^*)$ : it is the *discrete space*. So on the other hand this space consists of not isolated points, one will take $\subseteq \mathbb{R}^n$ : it is *continuous space*.

One will have in addition to specify contours and the characteristics of space X (limited, not limited, border, homogeneous, heterogeneous, explicit, stable, etc).

**Remark 3.1.** If one has to make with a profile being held in in continuous time and however presenting one or more instantaneous processes i.e. being held in discrete time, one will take $T = T1 \cup T2$ with

$$T1 \subset \mathbb{N}, T2 \subset \mathbb{R}^+, \text{so that } T1 \cap T2 = \emptyset.$$

**Remark 3.2.** If one has to make with one profiles being held in a partially heterogeneous space, one will take $X = X1 \cup X2$ with $X1 \subset \mathbb{N}^*(n \in \mathbb{N}^*)$, $X2 \subset \mathbb{R}^n$, so that $X1 \cap X2 = \emptyset$.

### 3.3.3. Choice of the Variables of State

Any mathematical model must emphasize the great phases of the profile and that materializes by the choice of the variables of state.

**Definition 3.3.** The variables of states of a dynamic profile are quantities dependant on the time whose causes are either given or unspecified. These variables of state represent the great phases of the profile and are such as their knowledge at a moment given $t_0$ makes it possible to predict the state of the profile at any moment $t \geq t_0$.

**Remark 3.4.** The choice of spaces of state, of time as well as the description of the variables of state belongs to the assumptions of modeling.

## 3.4. Formulation of the Model

The mathematical model is obtained by the expression of temporal dynamics of various variables of state to which one joint of the particular conditions checked by the profile.

If Y (t) then indicates the measurement of a variable of state Y at time t, the temporal dynamics of Y quite simply amounts expressing Y (t + Δt) according to Y (t) where Δt > 0. For that one with the following general relation :

$$Y(t + \Delta t) = Y(t) + E - S \qquad (3.1)$$

***E*** =Entry and ***S*** =Exit here represents all the entries and all the exits having taken place during time Δt in the phase Y of the profile.

Sometimes, the relation (3.1) are obtained by indicating the state Y by a rectangle (or a circle), the entries with the phase Y by entering arrows and the exits by the outgoing arrows of the rectangle. This technique of obtaining the relation (3.1) is known in the literature under the name of compartmental modeling.

According to discrete nature or continues spaces of time and state, the relation (3.1) led to dynamical systems described by table 1.

**Table-1.** Dynamical system resulting from the nature of spaces of time and state

| Time | Space | Dynamical system |
|---|---|---|
| **Continuous** | Continuous and heterogeneous | Partial diff. equation (PDE) |
| **Continuous** | Continuous and homogeneous | Ordinary diff. equation (ODE) |
| **Continuous** | Discrete | ODE |
| **Discrete** | Continuous (homog. or hetero.) | Difference equation (DE) |
| **Discrete** | Discrete | DE |
| **Discrete + Continuous** | Continuous and homogeneous | DE + ODE |
| **Discrete + Continuous** | Continuous and hetero. (partially) | DE + PDE |

**Remark 3.5.** Once the model formulated , it is necessary to carry out its mathematical analysis. This stage generally consists in seeing whether the formulated model is well or badly posed within the meaning of Hadamard [7] and to make as a dynamical system its qualitative study (research of the invariant sets and study of stabilities).

### 3.5. Validation of the Model

The formulation of a mathematical model generally reveals in addition to the variables of state, the parameters of three orders being able to depend on time and possibly on space. It acts:
(i) Constants which govern the profile and thus the values are universally known.
(ii) Coefficients whose role within the theoretical framework is well under- stood but for which the numerical values can vary according to the configuration and the conditions current of realization of the profile.
(iii) Coefficients of which the theoretical framework has little or nothing to say on their numerical values.
A mathematical model is known as valid when it adapts to the data (partial) available i.e the available data must make it possible to numerically estimate the values of the unknown parameters of the model (those of which - it is question with (ii) and (iii) above).

## 4. Mathematical Models and Numerical Simulations

If the mathematical analysis of a model explicitly makes it possible to have the exact mathematical solution of this model, then the use of this solution makes it possible to carry out not only predictions, but also to control the profile. The predictions resulting from the mathematical solution and the available data must be sufficiently close at the point to satisfy the modeler : it is the *test of the model*. If such is not the case, the model must be refined.

Unfortunately, for the majority of the mathematical models obtained with resulting from the modeling of a real phenomenon, the explicit solution is generally not accessible and fortunately, there is the computers.

The numerical simulations play a key role when the exact mathematical solution of the model is not known, in the sense that they constitute an artificial construction, intended to imitate the natural phenomenon or due to the industry of the man, with such an exactitude that one can mistake between reality and the numerical model. [8]

The principle to carry out simulations is simple. It is necessary to start by rewriting the mathematical model (if it is not it yet) in spaces of state and time of the computer which are all the two discrete ones : it is the discretization of the model which leads to the numerical model still called model of simulation.

Once the numerical model obtained, it should be implemented in the machine via a suitable software. One must then carry out several simulations which must confirm the theoretical results obtained during the analysis of the mathematical model, and, to allow to make predictions on the profile, together of things likely to suggest a control of the profile.

## 5. Application to Epidemiologic Modeling

### 5.1. Assumptions of Modeling

#### 5.1.1. Identification of the Epidemiologic Profiles

The parasitic cycle can be more or less complicated but implies, in all the cases, three essential stages:

The first is the *infection* during which the parasite penetrates inside (or clings on) its host.

The second is *the multiplication* where the parasite reproduces (sexually or non sexually) inside (or on) its host.

The last is *the spread* where the descendants of the parasite leave their host to infect others of them.

These three stages all are necessary to the life cycle of the parasite.

Epidemiology is the science of the epidemics, i.e the science of the contagious diseases which tackles a great number of individuals at the same time.

Thus, taking into account the three minimal stages of a parasitic cycle, the possible profiles in the modeling of an epidemic are the following:
*Profile 1: process of infection inter - host.*
*Profile 2: process of spread inter - host.*
*Profile 3: process of multiplication parasitic intra - host.*
*Profile 4: process of infection/spread inter - host.*
*Profile 5: process of infection/multiplication inter and intra - host.*
*Profile 6: process of multiplication/spread intra and inter - host.*
*Profile 7: process of infection/multiplication/spread inter and intra -host.*
In the description of the various profiles, it is important to clarify inter alia the following elements:
(i) Biological mechanisms of the disease corresponding with the profile selected.
(ii) Modes of transmission (selected) of the disease (vertical i.e. of the mother to her offspring, horizontal i.e by contact direct enters an individual not infected and an infected individual, vectorial i.e in way indirect enters an infected individual and an individual not infected).
(iii) The general structure of the population of individuals (homogeneous in only one block, homogeneous by blocks (partial heterogeneity), all the individuals are different (total heterogeneity), size (constant or not), insulated, taken into account of the mobility of the individuals, etc).

#### 5.1.2. Identification of the Dynamism of the Profile

Epidemiology is interested primarily in the variation of the number of cases according to time (and possibly of space). This implies that the epidemiologic profiles are basically dynamic, and consequently, the epidemics are mathematically modeled by dynamical systems (T, X, A, S).

### 5.1.3. Choice of Spaces of State and Time

Space time to choose must be that in which the profile takes place and not that in which the data are collected.

Thus if the profile takes place in real-time one takes $T \subseteq \mathbb{R}^+$. So on the other hand the profile takes place in discrete time one will take $T \subseteq \mathbb{N}$.

In the same way, the space of state is the physical space which shelters the population. It must clearly be definite (continuous, discrete, limited, not limited, border, homogeneous, heterogeneous, explicit, stable, etc).

### 5.1.4. Choice of the Variables of State

The variables of state which are quantities must describe the great stages by which the disease within the population forwards. In general and that is not exhaustive, six stages (not inevitably all, that is function of the disease) are considered.

The susceptible (S) who are the healthy individuals but who can be contaminated, the exposed (E) who are the individuals carrying the disease but are noninfectious (i.e cannot transmit the disease), the infected (I) who are the infectious individuals, the deceased (D) who are the individuals having succumbed to the disease, the immunized (M) who are the individuals immunized against the disease, the latent (L) who are the individuals carrying the disease but not presenting any symptom.

In addition to that, if the contamination is indirect, variables of state describing the temporal dynamics of the pathogenic agent can be taken into account.

## 5.2. Formulation of the Model

It consists in defining the temporal dynamics of each variable of state. Let us recall that if Y (t) indicates the density (this term is employed when one is in so much continuous. In discrete time one quite simply says the number of individuals) of a variable of state Y to time t then, the temporal dynamics of Y quite simply amounts expressing Y (t + Δt) according to Y (t) where Δt > 0. For that one with the following general relation:

$$Y\,(t + \Delta t) = Y\,(t) + E - S \qquad (5.1)$$

The possible entries and exits here are given by the description of the biological mechanisms of the profile making it possible to pass from a stage of the disease to another, like, by the dynamic ones taking place within the population (births, death, mobility). The technique of compartmental modeling is particularly advised here for the visualization of flows of biological exchanges possible between the various variables of state.

If the space of state is heterogeneous, the variables of state can depend in addition to the variable time t of the variable of space x. The choice of a deterministic model is generally made for populations of big size and the stochastic model for populations of small size.

A good control of the dynamics of the populations and certain physical laws in particular the law of action of mass are essential for a good formulation of the model. Let us recall finally to finish that the formulated model must be valid and that it is important to see essential for the modeler to have a good control of the computer tools of its time.

# 6. Example: Modeling and Mathematical Analysis of an Influenza Epidemic in a Metapopulation in Discrete Time

## 6.1. Assumptions of Modeling

We give in this part basic assumptions allowing to obtain our model.

**Assumption (H1):** The individuals are allocated with a discrete space $\Omega \subset \mathbb{N}^d$ $(d = 1, 2, 3)$ heterogeneous, stable, subdivided out of n (n = 2, 3, ...) local populations (or sites) connected between them by migrations.

**Assumption (H2):** Sites of Ω are large enough to accommodate panmixis local populations, but not larger.

**Assumption (H3):** The population of a site of Ω is homogeneous and only the movements on broad scale between the various sites are spatially constrained, the displacement of an individual being dependent of its serologic statute i.e. an infected individual cannot move.

**Assumption (H4)**: The migration is only function of the distance.

## 6.2. Model of Migratory Movements

Let us note

- $X_i(t)$ the number of individuals in the population i at time $t$ $(i \in \{1, 2, \ldots n\};\ t \in \mathbb{N})$.
- $K(i,j)$ probability of migrating of the population i to the population j per unit of time, independently of the serologic statute of the individual.

One has then:

$$X_i(t+1) = X_i(t) + \sum_{j=1}^{n} X_j(t)K(j,i) - \sum_{j=1}^{n} X_i(t)K(i,j) \qquad (6.1)$$

The first sum corresponds to immigrations and the second with the emigrations and one can also note that $K(i,i) = 0\ (i = 1, 2, \ldots n)$. Like $K = \{K(i,j), i, j \in \{1, \ldots, n\}\}$are a probability distribution, one has:

$$\forall i,j \in \{1,\dots,n\},\quad 0 \le K(i,j) \le 1 \quad and \quad \sum_{i=1}^{n} K(i,j) = \sum_{j=1}^{n} K(i,j) = 1$$

K is then a kernel probability (see [21]) and one will call it kernel of migration.
Thus one has :

$$X_i(t+1) = X_i(t) + \sum_{j=1}^{n} X_j(t)K(j,i) - \sum_{j=1}^{n} X_i(t)K(i,j) \quad (6.2)$$

$$= X_i(t) + \sum_{j=1}^{n} X_j(t)K(j,i) - X_i(t)\sum_{j=1}^{n} K(i,j) \quad (6.3)$$

$$= X_i(t) + \sum_{j=1}^{n} X_j(t)K(j,i) - X_i(t) \quad (6.4)$$

$$= \sum_{j=1}^{n} X_j(t)K(j,i) \quad (6.5)$$

## 6.3. Local Model of Spread of Influenza

In this subsection, we modeled locally influenza spread within each site of Ω in absence of the migratory movements.

We consider a human population that we subdivide into four explicit, disjoint disease states within each site i = 1, 2, ..., n, which are as follows :

$S_i(t)$ = density of susceptible individuals on time $t \in \mathbb{N}$.
$E_i(t)$ = density of latent (incubating) individuals on time t.
$I_i(t)$ = density of infectious (iii) individuals on time t.
$R_i(t)$ = density of recovered individuals on time t.

The size of the population of site i at time t is given by $N_i(t) = S_i(t) + E_i(t) + I_i(t) + R_i(t)$.

One supposes that for each site i, the population is of constant size, i.e. the births are equal to the death. The four quantities $S_i$, $E_i$, $I_i$, and $R_i$ are the dependent variables of the local model.

Natural death is assumed to be independent of disease status with rate constant di and following the Hyman and Laforce model [9] there is no death due to influenza.

It is supposed newborn are susceptible and are not infected with flu. The only voice of infection of the Susceptible individuals ($S_i$) it is its contact with an infectious individual ($I_i$) (direct transmission). The rate of contact between susceptible and infectious individual is noted $\beta_i$ and can depend on time. The latent individuals become infectious at a rate γ. Infectious (iii) individuals cure at a rate α and the recovered individuals becomes again susceptible at a rate w.

The above assumptions lead to the following system of 4n difference equations for each site i = 1, 2, ..., n of Ω :

$$\begin{cases} S_i(t+1) = S_i(t) + d_i\big(N_i(t) - S_i(t)\big) - \beta_i(t)S_i(t)I_i(t) + wR_i(t) \\ E_i(t+1) = E_i(t) + \beta_i(t)S_i(t)I_i(t) - (d_i+\gamma)E_i(t) \\ I_i(t+1) = I_i(t) + \gamma E_i(t) - (d_i+\alpha)I_i(t) \\ R_i(t+1) = R_i(t) + \alpha I_i(t) - (d_i+w)R_i(t) \end{cases} \quad (6.6)$$

The initial conditions are given by $S_i(0) = S_0$, $E_i(0) = E_0$, $I_i(0) = I_0$ and $R_i(0) = R_0$.

## 6.4. General Model of Spread of Influenza

By uniting models (6.5) and (6.6), one obtains the following general model for each site i = 1, 2, ..., n of Ω :

$$\begin{cases} S_i(t+1) = S_i(t) + d_i\big(N_i(t) - S_i(t)\big) - \beta_i(t)S_i(t)I_i(t) + wR_i(t) + \sum_{j=1}^{n} S_j(t)K(j,i) \\ E_i(t+1) = E_i(t) + \beta_i(t)S_i(t)I_i(t) - (d_i+\gamma)E_i(t) \\ I_i(t+1) = I_i(t) + \gamma E_i(t) - (d_i+\alpha)I_i(t) \\ R_i(t+1) = R_i(t) + \alpha I_i(t) - (d_i+w)R_i(t) + \sum_{j=1}^{n} R_j(t)K(j,i) \\ S_i(0) = S_0,\ E_i(0) = E_0,\ I_i(0) = I_0,\ R_i(0) = R_0 \end{cases} \quad (6.7)$$

For each site i = 1, 2, ..., n of Ω, the total population is governed by the following difference equation :

$$N_i(t+1) = N_i(t) + \sum_{j=1}^{n} (S_j(t) + R_j(t))K(j,i) \quad (6.8)$$

Let us note that the model (6.7) is valid because the new cases of influenza (available data) are represented by the term $f_i(t) = \beta_i(t)S_i(t)I_i(t)$ in (6.7) and consequently the statistical fitting of the new cases will make it possible to obtain the term fi(t), then, one can thanks to simulations estimate the contact rate $\beta_i(t)$ numerically. In the same way the probabilities K(j,i) can be estimated thanks to the data on the immigrations (available data) represented by the term $\sum_{j=1}^{n}(S_j(t) + R_j(t))K(j,i)$ of (6.8). The other values of the parameters are known.

## 6.5. Existence of a Unique Solution of the Model (6.7)

We have the following result :

**Theorem 6.1**. For each i = 1, 2, ..., n, the system (6.7) admits a unique solution

$x_i(t) = \begin{pmatrix} S_i(t) \\ E_i(t) \\ I_i(t) \\ R_i(t) \end{pmatrix} \in \mathbb{R}^4$ $(t \in \mathbb{N})$ who depends continuously on the initial condition $x_i(0)$.

***Proof.*** *For each i = 1, 2, ..., n, let us pose* $x_i(t) = \begin{pmatrix} S_i(t) \\ E_i(t) \\ I_i(t) \\ R_i(t) \end{pmatrix} \in \mathbb{R}^4$ $(t \in \mathbb{N})$ *and consider function*

$f_i\ :\ \mathbb{N} \times \mathbb{R}^4 \to \mathbb{R}^4$ defines

$$f_i(t, x_i(t)) = \begin{pmatrix} d_i(N_i(t) - S_i(t)) - \beta_i(t)S_i(t)I_i(t) + wR_i(t) + \sum_{j=1}^{n} S_j(t)K(j,i) \\ \beta_i(t)S_i(t)I_i(t) - (d_i + \gamma)E_i(t) \\ \gamma E_i(t) - (d_i + \alpha)I_i(t) \\ \alpha I_i(t) - (d_i + w)R_i(t) + \sum_{j=1}^{n} R_j(t)K(j,i) \end{pmatrix}$$

Then the model (6.7) is written for each i = 1, 2, ..., n

$$\begin{cases} x_i(t+1) & = x_i(t) + f_i(t, x_i(t)) \\ x_i(0) = & x_0 \end{cases} \qquad (6.9)$$

By carrying out t iterations, one has according to (6.9) :

$$\begin{array}{ll} x_i(1) & = x_i(0) + f_i(0, x_i(0)) \\ x_i(2) & = x_i(1) + f_i(1, x_i(1)) \\ \vdots & \vdots \\ x_i(t-1) & = x_i(t-2) + f_i(t-1, x_i(t-1)) \\ x_i(t) & = x_i(t-1) + f_i(t, x_i(t)) \end{array}$$

what leads us after summation to

$$x_i(t) = x_0 + \sum_{j=0}^{t} f_i(j, x_i(j)) \qquad (6.10)$$

□

## 6.6. Equilibria and Stability

In this section, we study for each site i = 1, 2, ..., n of Ω, solutions of model (6.7) in which

$$\begin{pmatrix} S_i(t+1) \\ E_i(t+1) \\ I_i(t+1) \\ R_i(t+1) \end{pmatrix} \equiv \begin{pmatrix} S_i(t) \\ E_i(t) \\ I_i(t) \\ R_i(t) \end{pmatrix} \equiv \begin{pmatrix} S_i^* \\ E_i^* \\ I_i^* \\ R_i^* \end{pmatrix}$$

is independent of the time t.

### 6.6.1. Equilibria

For contact rate $\beta_i(t) \equiv \beta_i$ for all t ∈ N and each site i = 1, 2, ..., n of Ω, equilibrium $(S_i^*, E_i^*, I_i^*, R_i^*)$ of system (6.7) must satisfy the system

$$\begin{cases} d_i(N_i - S_i^*) - \beta_i S_i^* I_i^* + wR_i^* + \sum_{j=1,j\neq i}^n S_j^* K(j,i) = 0, \\ \beta_i S_i^* I_i^* - (d_i + \gamma)E_i^* = 0, \\ \gamma E_i^* - (d_i + \alpha)I_i^* = 0, \\ \alpha I_i^* - (d_i + w)R_i^* + \sum_{j=1,j\neq i}^n R_j^* K(j,i) = 0. \end{cases} \quad (6.11)$$

Let us pose

$$m_1 = \sum_{j=1,j\neq i}^n S_j^* K(j,i) \text{ and } m_2 = \sum_{j=1,j\neq i}^n R_j^* K(j,i).$$

We have the following result

**Lemma 6.2.** For each site i = 1, 2, ..., n of Ω, the disease - free equilibrium of system (6.7) is given by

$$u_i^0 = (S_i^{0,*}, 0, 0, R_i^{0,*})$$

and the endemic equilibrium by

$$u_i^1 = (S_i^{1,*}, E_i^{1,*}, I_i^{1,*}, R_i^{1,*})$$

Where

$$S_i^{0,*} = \frac{1}{d_i}(d_i N_i + \frac{wm_2}{d_i+w} + m_1),\ R_i^{0,*} = \frac{m_2}{d_i+w},\ S_i^{1,*} = \frac{(d_i+\alpha)(d_i+\gamma)}{\gamma\beta_i},$$
$$E_i^{1,*} = \frac{d_i+\alpha}{\gamma} I_i^{1,*},\ R_i^{1,*} = \frac{1}{d_i+w}(\alpha I_i^{1,*} + m_2) \text{ and}$$
$$I_i^{1,*} = \frac{\gamma d_i N_i \beta_i (d_i+w) - d_i(d_i+\alpha)(d_i+\gamma)(d_i+w) + w\gamma\beta_i m_2 + m_1\gamma\beta_i(d_i+w)}{\beta_i[(d_i+\alpha)(d_i+\gamma)(d_i+w) - \alpha w\gamma]}$$

***Proof***. *The second equation of (6.11) makes it possible to write*

$$E_i^* = \frac{1}{d_i+\gamma}\beta_i S_i^* I_i^* \quad (6.12)$$

*(6.12) in the third equation leads to*

$$I_i^* = 0 \quad (6.13)$$

*Or*

$$S_i^* = \frac{(d_i+\alpha)(d_i+\gamma)}{\gamma\beta_i} \quad (6.14)$$

*For $I_i^* = 0$, the resolution of the system (6.11) makes it possible to Obtain*

$$E_i^* = 0 \quad (6.15)$$

$$R_i^* = \frac{m_2}{d_i+w} \quad (6.16)$$

*and*

$$S_i^* = \frac{1}{d_i}(d_i N_i + \frac{wm_2}{d_i+w} + m_1) \quad (6.17)$$

*from where obtaining disease - free equilibrium $u_i^0 = (S_i^{0*}, 0, 0, R_i^{0,*})$ thanks to (6.17), (6.15), (6.13) and (6.16).*

*For*

$$S_i^* = \frac{(d_i+\alpha)(d_i+\gamma)}{\gamma\beta_i}$$

*the fourth equation of (6.11) makes it possible to draw*

$$R_i^* = \frac{1}{d_i+w}(\alpha I_i^* + m_2) \quad (6.18)$$

*(6.18) and (6.14) replaced in the first equation of (6.11) allows to have*

$$I_i^* = \frac{\gamma d_i N_i \beta_i (d_i+w) - d_i(d_i+\alpha)(d_i+\gamma)(d_i+w) + w\gamma\beta_i m_2 + m_1\gamma\beta_i(d_i+w)}{\beta_i[(d_i+\alpha)(d_i+\gamma)(d_i+w) - \alpha w\gamma]} \quad (6.19)$$

*It is clear that $I_i^* > 0$, from where obtaining endemic equilibrium $u_i^1 = (S_i^{1,*}, E_i^{1,*}, I_i^{1,*}, R_i^{1,*})$ thanks to (6.14), (6.12), (6.19) and (6.18).*

### 6.6.2. Stability of Disease - Free Equilibrium

For each site i = 1, 2, ..., n of Ω, the model (6.9) is written

$$\begin{cases} x_i(t+1) &= g_i(t, x_i(t)) \\ x_i(0) = & x_0 \end{cases} \quad (6.20)$$

Where $g_i(t, x_i(t)) = x_i(t) + f_i(t, x_i(t))$.
The jacobian matrix of $g_i(t, x_i(t))$ at the disease - free equilibrium $u_i^0 = (S_i^{0*}, 0, 0, R_i^{0,*})$ is given by

$$A(t) = \begin{pmatrix} 1-d_i & 0 & -\beta_i(t)S_i^{0,*} & w \\ 0 & 1-d_i-\gamma & \beta_i(t)S_i^{0,*} & 0 \\ 0 & \gamma & 1-d_i-\alpha & 0 \\ 0 & 0 & \alpha & 1-d_i-w \end{pmatrix}$$

Thus, by linearizing (6.20) around $u_i^0$ (see [24]) , we have

$$\begin{cases} x_i(t+1) & = A(t)x_i(t) + \tilde{g}_i(t, x_i(t)) \\ x_i(0) = & x_0 \end{cases} \qquad (6.21)$$

Where

$$\tilde{g}_i(t, x_i(t)) = \begin{pmatrix} d_i N_i(t) - \beta_i(t)I_i(t)(S_i(t) - S_i^{0,*}) + \sum_{j=1}^n S_j K(j,i) \\ \beta_i(t)I_i(t)(S_i(t) - S_i^{0,*}) \\ 0 \\ \sum_{j=1}^n R_j K(j,i) \end{pmatrix}$$

The main result of this subsection is the following :

**Lemma 6.3.** For each site i = 1, 2, ..., n of Ω, the disease - free equilibrium $u_i^0 = (S_i^{0*}, 0, 0, R_i^{0,*})$ of model (6.7) is exponentially stable if and only if $R_0 < 1$ and unstable if and only if $R_0 > 1$.
With

$$R_0 = \frac{\beta_i(t)S_i^{0,*}}{\alpha} \qquad (6.22)$$

***Proof.*** *For all $t \in N$ and each site i = 1, 2, ..., n of Ω, it is checked easily that $g_i(t, u_i^0) = u_i^0$. Thus, the stability of $u_i^0$ is determined by that of the linear part of (6.21) [10]. Following simple algebraic handling, one establishes that the eigenvalues of A(t) is given by :*

$$\lambda_1 = 1 - d_i,\ \lambda_2 = 1 - d_i - w,\ \lambda_3 = 1 - d_i - \frac{\alpha+\gamma+\sqrt{\Delta}}{2} \text{ and}$$
$$\lambda_4 = 1 - d_i - \frac{\alpha+\gamma-\sqrt{\Delta}}{2} \text{ with } \Delta = (\alpha-\gamma)^2 + 4\gamma\beta_i(t)S_i^{0,*}.$$

*It is clear that $\lambda_1 < 1$, $\lambda_2 < 1$ and $\lambda_3 < 1$. Concerning $\lambda_4$, let us notice that*

$$\Delta - (\alpha+\gamma)^2 = 4\alpha\gamma\left(\frac{\beta_i(t)S_i^{0,*}}{\alpha} - 1\right)$$

*Thus while posing*

$$R_0 = \frac{\beta_i(t)S_i^{0,*}}{\alpha},$$

*one has $\lambda_4 < 1 \Leftrightarrow R_0 < 1$ and $\lambda_4 > 1 \Leftrightarrow R_0 > 1$. Consequently,*
*$\rho(A(t)) < 1 \Leftrightarrow R_0 < 1$ and $\rho(A(t)) > 1 \Leftrightarrow R_0 > 1$, i.e. for the linear part of (6.21), ui0 is asymptotically stable if and only if $R_0 < 1$ and unstable if and only if $R_0 > 1$.*
*Moreover, since $\tilde{g}_i(t, x_i(t)) = o(\|u_i^0\|)$ uniformly as $\|x\| \to 0$, one deduces ( [10] Theorem 6.6.1 and 6.6.2) that $u_i^0$ is exponentially stable if and only if $R_0 < 1$ and unstable if and only if $R_0 > 1$.*

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