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Modeling epidemics by means of the stochastic description of complex systems

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Abstract

The aim of this article is to show a way in which the problem of predicting the evolution of an epidemic may be tackled by describing it in the framework of Boltzmann's kinetic theory, as it has been developed and applied in the last years to complex systems by a suitable modification of the Boltzmann equation, via a suitable reinterpretation of state variables and the introduction of the notion of «functional subsystems». Accordingly, in this article we model an arbitrary (national) population *S* as a complex system, split in two functional subsystems, the first containing all single individuals of *S* and the second containing the «care tools», that are to be meant as available places in hospitals with a sufficient number of physicians and of equipments for intensive cares. The state variable on the first subsystem will be the «health state», and the state variable on the other will be the «effectiveness». We shall then write a system of nonlinear ordinary differential equations which gives the evolution of the probability distribution on the set of possible values of the health states. By assigning data partly on the basis of plausibility assumptions and partly as estimated from those furnished by institutions of Campania region, the system takes a form allowing the numerical simulation of such evolution, which will be performed and presented in a forthcoming paper.

KEYWORDS

active particles, complex systems, kinetic theory, mathematical models, probability

1 | INTRODUCTION

The problem of predicting, and if possible at least slowing down, the spread of an epidemic has been in the last year, and will be in the next months until the vaccination campaign will have reached at least three quarters of the whole population, the hottest problem all mankind has found itself in the need to face. Any delay in stopping the present COVID-19 epidemics, any error in the prediction of its evolution would unavoidably lead to devastating consequences, not only in connection with the economic conditions of each nation hit by this epidemic, but also in connection with psychological conditions of its members, and even with their social relationships and their mutual behaviors.

Now, to predict the evolution of any epidemic is a task of epidemiology, and the fundamental role of statistical and stochastic models in the achievement of this goal is so widely acknowledged in the literature that it is almost impossible to give exhaustive bibliographic references (see, e.g., References 1-5). All the information that can be obtained about the diffusion rate of an infectious disease or about its lethality, must be obtained from the statistical study of its diffusion[6-17] and of the percentage of its victims in a suitably defined «initial period» or from the same statistical study of previous infections of the same kind. But it is also well known that such kind of statistical studies can only lead to short term estimates of percentages of infected individuals or victims.[11,18-21] A more effective use of Statistics, which could deliver long-term predictions of both percentages of infected people and victims, should be based on evolution equations for these percentages—or, what is the same, for the probability of any member of the population to be infected or even killed by the infectious agent. This has led to a large number of studies based on kinetic models[16,22-31] and, in particular on the analysis of a suitably defined stochastic process.[15]

In this connection, the main aim of this article is to develop the general description proposed in Reference 23 (and discussed in more theoretical terms in Reference 24), as a tool to include statistical information in the formulation of a general evolution equation obtained in the framework of the Kinetic Theory for Active Particles (KTAP), a theoretical scheme which can be readily seen to produce the above quoted kinetic models[16,22,25-31] as particular and simplified cases, which is based on Vlasov's generalization of the Boltzmann equation for the Kinetic Theory of Gases[24,32,33] and has already been used in a large number of papers to give a formal statement and a hint toward a solution for medical, biological and also psychological problems (see e.g., References 34-37, also for more complete bibliographic references). We apply it to a typical national society represented as a complex system whose behavior can be predicted only by assigning a probability distribution on the consequences of interactions between its members, not only (or not mainly) in order to obtain the evolution of the relative frequencies of infected people at different severity degrees, but above all in order to study the interactions between infected people and care structures, the time at which these latter will be exhausted under different initial conditions and different assumptions on the diffusion rate of the disease, and the effects of the emergency containment measures. This problem has been already tackled in a number of interesting papers,[17,19,38-46] but the aim of this article, as we shall argue in more details, can be described as twofold: on one hand, to show that KTAP seem particularly powerful and complete in the mathematical description of an epidemics; on the other hand, since KTAP makes use of parameters that cannot be evaluated in terms of official data, to suggest that the repeated application of its scheme to different systems of arbitrarily assigned values of parameters could lead to estimate them as accurately as possible by a forward-backward procedure. This point will be briefly discussed as a research perspective in Section 4.

Now, to achieve our goals, since the above outlined problem is strictly connected with the mathematical problem of stability of solutions with respect to changes of parameters,[47] it is almost unavoidable to analyze the dependence of solutions on parameters by referring to numerical simulations, as already done in almost all the papers quoted above. Unfortunately, in view of the large size of the system obtained here (15 equations for 15 unknown probability distribution functions), these simulations cannot be performed here, and need to be postponed to a next paper. We shall outline the formal structure of the theory in Section 2, referring the reader for details to the papers in the bibliography; in Section 3, we specialize the model delivered by the theory to the case of the present COVID epidemics, by using some statistical data obtained from official institutional reports together with plausible assumptions about the social behavior of the members of the considered society (in a forthcoming paper, we shall perform the numerical simulations of the solutions of the equations, to give some examples of mathematical description—and, at need, prediction—of the evolution of the epidemics and, above all, of its consequences on the care structures with and without containment measures). Finally, in the last section, we offer some conclusions together with some perspectives for future research to precise the results of this article and to obtain more accurate results on the basis of a more complete and precise statistical information.

2 | THE MATHEMATICAL FRAMEWORK

A *complex system* is a set S of a very large number of objects (that can represent particles of a mechanical systems, cells, living individuals, or human beings) called *individuals* or *active particles*. The *state* of each individual in S is defined according to the context in which we aim to develop our description, and can be expressed as a scalar variable u or a vector variable $\mathbf{u} \equiv (u^1, u^2, \dots, u^m)$ which, much more for historical reasons than for reasons suggested by the context, is called *activity* or — more simply — *state variable*. This variable may describe the kinetic state of a material particle, or the activity of a cell in its interactions with other cells of a different tissue, or the health state of a living individual, or the level of wealth and the social condition of a human being in a collectivity. According to the context, the activity may be assumed to take its values in a *discrete* domain (typically, a finite or countable subset of $\mathbb{Z}$ or $\mathbb{Z}^m$) or in a *continuous* domain (typically, a bounded or unbounded real interval or a bounded or unbounded domain of $\mathbb{R}^m$). In any case, the domain D_u (or $D_{\mathbf{u}}$) in which the state variable is allowed to take its values is called the *state space* of the system.

The viewpoint from which the mathematical framework is developed is statistical, as in Boltzmann's Kinetic Theory of Gases: this means that we are interested to describe the evolution in time of the system as a whole rather than the way in which the states of single particles vary with time. More precisely, we are aware that any precise description of the state of each particle of S must be given up, for both theoretical and practical reasons,[32,33] so we decide to study the relative frequency (or probability) distribution over the state space at each instant. In other words, the state variable is conceived as a *random variable* and the goal of the study becomes the forecast of the evolution of its probability density function as well as of some of its parameters (expected value, moment of order two, standard deviation).

In many cases of interest, S is considered to be split into a family $\{S_1, S_2, \dots, S_k\}$ of subsystems, called its *functional subsystems*. The introduction of such subsystems aims to describe the interactions between different classes of individuals with different reactions to interactions and finds its natural application in biology, for instance to describe the fight between tumor cells and immune system, or the competition between different species to model Darwinian selection, or in social sciences, to model interactions between social classes, or in economics, to model the fluxes of wealth, for example, between the class of financial managers, that of entrepreneurs and that of salaried workers. In some cases, the same variable can be used to identify the state of the members of all the functional subsystems, but in other cases different state variables must be used for different subsystems.

In this section, we shall describe in some details the case of a system S consisting in four different subsystems S_1, S_2, S_3 and S_4 such that the state of individuals in each S_h is described by a different *discrete* scalar variable u_h. We set

$$D_h = \{u_{h,1}, u_{h,2}, \dots, u_{h,m_h}\}.$$

For any t in a time-interval $\mathbb{I} \subseteq \mathbb{R}$, the state of subsystem S_h at time t will be identified by a probability distribution (also called *state vector*) $\mathbf{f}_t^{(h)} \equiv (f_t^{(h)}(u_{h,1}), f_t^{(h)}(u_{h,2}), \dots, f_t^{(h)}(u_{h,m_h}))$ on D_h, and, for any $k \in \{1, 2, \dots, m_h\}$, we can define the function $f_k^{(h)} \ : \ t \in \mathbb{I} \rightarrow f_k^{(h)}(t) \equiv f_t^{(h)}(u_{h,k}) \in [0, 1]$. According to this definition we have

$$\sum_{k=1}^{m_h} f_k^{(h)}(t) = \sum_{k=1}^{m_h} f_t^{(h)}(u_k) = 1, \quad \forall\, h \in \{1, 2, 3, 4\}.$$

The expected values of the distributions $\mathbf{f}_t^{(h)}$, for any t, will be

$$E_h[u_h](t) = \sum_{k=1}^{m_h} u_{h,k} f_k^{(h)}(t),$$

and we consider also their second-order moments

$$E_h[u_h^2](t) = \sum_{k=1}^{m_h} u_{h,k}^2 f_2^{(h)}(t),$$

that play in the general context the same role as temperature in statistical thermomechanics of gases. It is also often useful, in the analysis and solution of problems about the determination and the comparison of the distributions $f_2^{(h)}(t)$ in a time-interval (see below), to consider also higher order moments

$$E_h[u_h^p](t) = \sum_{k=1}^{m_h} u_{h,k}^p f_k^{(h)}(t)$$

with $p \geq 3$.

Now, the evolution of the system S is envisaged as a time-continuous stochastic process, and the time derivative of each probability function $f_k^{(h)}$ is expressed, according to the law of alternatives, in terms of transition probabilities. More precisely,

1. for any $(r, s, j) \in \{1, 2, \dots m_h\}^3$, the symbol $F^r{}_{sj}(h) \equiv F_h(u_{h,s}, u_{h,j}; u_{h,r})$ will denote the probability that a particle of S_h *falls* from the state $u_{h,s}$ into the state $u_{h,r}$ after an interaction with another particle of S_h which is in the state $u_{h,j}$: accordingly,

$$\sum_{r=1}^{m_h} F^r{}_{sj}(h) = 1, \quad \forall\ (s,j) \in \{1,2,\ \dots, m_h\}^2,\ \forall\ h \in \{1,2,3,4\}.$$

2. for any $(r,s) \in \{1,2,\ \dots\ m_h\}^2$, and for any $j \in \{1,2,\ \dots, m_k\}$ (with $k \neq h$), the symbol $\Phi^r{}_{sj}(h,k) \equiv \Phi_{hk}(u_{h,r}, v_{k,j}; u_{h,s})$ will denote the probability that a particle of S_h *falls* from the state $u_{h,s}$ into the state $u_{h,r}$ after an interaction with a particle of S_k which is in the state $v_{k,j}$: accordingly,

$$\begin{aligned}&\sum_{r=1}^{m_h} \Phi^r{}_{sj}(h,k) = 1, \quad \forall\ s \in \{1,2,\dots, m_h\},\ \forall j \in \{1,2,\dots, m_k\},\\ &\forall\ h \in \{1,2,3,4\},\ \forall\ k \neq h.\end{aligned}$$

Thus, using the law of alternatives, we write the following system of differential equations

$$\begin{aligned}
\frac{\mathrm{d}f_h^{(1)}}{\mathrm{d}t}(t) = &\sum_{i,j}^{1\dots m_1} \tau_{ij}^1 F^h{}_{ij}(1) f_i^{(1)}(t) f_j^{(1)}(t) - \sum_{i,j}^{1\dots m_1} \tau_{hj}^1 F^i{}_{hj}(1) f_h^{(1)}(t) f_j^{(1)}(t) +\\
&+ \sum_{k=2}^{4} \left[\sum_{i=1}^{m_1} \sum_{j=1}^{m_1} \eta_{ij}^{1k} \Phi^h{}_{ij}(1,k) f_i^{(1)}(t) f_j^{(k)}(t) + \right.\\
&\left. - \sum_{i=1}^{m_1} \sum_{j=1}^{m_k} \eta_{hj}^{1k} \Phi^i{}_{hj}(1,k) f_h^{(1)}(t) f_j^{(k)}(t) \right], \qquad (h = 1,2,\ \dots, m_1)\\
\frac{\mathrm{d}f_h^{(2)}}{\mathrm{d}t}(t) = &\sum_{i,j}^{1\dots m_2} \tau_{ij}^2 F^h{}_{ij}(2) f_i^{(2)}(t) f_j^{(2)}(t) - \sum_{i,j}^{1\dots m_k} \tau_{hj}^2 F_{hj}^i(2) f_h^{(2)}(t) f_j^{(2)}(t) +\\
&+ \sum_{k\neq 2}^{1\dots 4} \left[\sum_{i=1}^{m_2} \sum_{j=1}^{m_k} \eta_{ij}^{2k} \Phi^h{}_{ij}(2,k) f_i^{(2)}(t) f_j^{(k)}(t) + \right.\\
&\left. - \sum_{i=1}^{m_2} \sum_{j=1}^{m_k} \eta_{hj}^{2k} \Phi_{hj}^i(2,k) f_h^{(2)}(t) f_j^{(k)}(t) \right], \qquad (h = 1,2,\ \dots, m_2)\\
\frac{\mathrm{d}f_h^{(3)}}{\mathrm{d}t}(t) = &\sum_{i,j}^{1\dots m_3} \tau_{ij}^3 F^h{}_{ij}(3) f_i^{(3)}(t) f_j^{(3)}(t) - \sum_{i,j}^{1\dots m_3} \tau_{hj}^3 F_{hj}^i(3) f_h^{(3)}(t) f_j^{(k)}(t) +\\
&+ \sum_{k\neq 3}^{1\dots 4} \left[\sum_{i=1}^{m_3} \sum_{j=1}^{m_k} \eta_{ij}^{3k} \Phi^h{}_{ij}(3,k) f_i^{(3)}(t) f_j^{(k)}(t) + \right.\\
&\left. - \sum_{i=1}^{m_3} \sum_{j=1}^{m_k} \eta_{hj}^{3k} \Phi_{hj}^i(3,k) f_h^{(3)}(t) f_j^{(k)}(t) \right], \qquad (h = 1,2,\ \dots, m_3)\\
\frac{\mathrm{d}f_h^{(4)}}{\mathrm{d}t}(t) = &\sum_{i,j}^{1\dots m_4} \tau_{ij}^4 F^h{}_{ij}(4) f_i^{(4)}(t) f_j^{(4)}(t) - \sum_{i,j}^{1\dots m_4} \tau_{hj}^4 F_{hj}^i(4) f_h^{(4)}(t) f_j^{(4)}(t) +\\
&+ \sum_{k=1}^{3} \left[\sum_{i=1}^{m_4} \sum_{j=1}^{m_k} \eta_{ij}^{4k} \Phi^h{}_{ij}(4,k) f_i^{(4)}(t) f_j^{(k)}(t) + \right.\\
&\left. - \sum_{i=1}^{m_4} \sum_{j=1}^{m_k} \eta_{hj}^{4k} \Phi_{hj}^i(4,k) f_h^{(4)}(t) f_j^{(k)}(t) \right], \quad (h = 1,2,\ \dots, m_4),
\end{aligned} \tag{1}$$

where, for any $k \in \{1,2,3,4\}$ and any $(r,s) \in \{1,2,\ \dots, m\}^2$, $\tau_{rs}^k \equiv \tau(u_{k,r}, u_{k,s})$ is the so-called *encounter rate* of particles of S_k in the states $u_{k,r}$ and $u_{k,s}$, that is the number of pairwise interactions between particles of S_k, that are in the states $u_{k,r}$ and $u_{k,s}$, per time unit, so that for any sufficiently small Δt the product $\tau_{rs}^k \Delta t$ is the probability that one such interaction occur in the time interval Δt *provided* the individuals involved belong to S_k are in the states $u_{k,r}$ and $u_{k,s}$ (accordingly, τ_{rs}^k

is in turn a *conditional* probability or, more precisely, the ratio of a conditional probability to time). Its presence in the first two terms at right-hand side of each equation of system (1)* is due to the fact that these terms express respectively the increase of probability of state $u_{k,h}$ as the probability that some «candidate» particles of S_2 in the state $u_{k,r}$ interact with some *field* particles of S_k in the state $u_{k,s}$ (and, as a consequence, fall in the state $u_{k,h}$ with a positive probability) and the decrease of probability of state $u_{k,h}$ as the probability that some «test» particles of S_k in the state $u_{k,h}$ interact with some *field* particles of S_k in the state $u_{k,s}$ (and, as a consequence, *leave* the state $u_{k,h}$ with a positive probability). The coefficients $\eta_{rs}^{\ell k}$ (for $r \in \{1, 2, \ldots, m\}$ and $s \in \{1, 2, \ldots, n\}$) in the other terms at right-hand sides of Equation 1 have the same meaning: for any ℓ and k $\eta_{rs}^{\ell k}$ is the *encounter rate* between any particle of S_ℓ which is in the state r and any particle of S_k which is in the state s.

Notice that the above form (1) is strictly related to the assumption that any change of state of a particle can occur *only* after an interaction, that is, no interaction implies no change of state (an assumption somehow recalling a kind of «inertia principle»). But, as we shall remark in the next Section (and is argued in a forthcoming paper[48]), such an assumption cannot be accepted in models of epidemics, in which *spontaneous* changes of state can occur at least in some functional subsystems (for instance, spontaneous healing). This will lead us to insert additional terms in one or more equations of System (1), in order to account for such effects. This point will be discussed in some details in Section 3.

For the sake of completeness, we recall that it is customary in the literature to write system (1) in the form

$$\frac{\mathrm{d}f_h^{(\ell)}}{\mathrm{d}t}(t) = J_h^{(\ell)}[f^{(1)},f^{(2)},f^{(3)},f^{(4)}](t) \qquad (h = 1, 2, \ \ldots, m_\ell; \ \ell = 1, 2, 3, 4), \tag{2}$$

where

$$\begin{aligned} J_h^{(\ell)}&[f^{(1)},f^{(2)},f^{(3)},f^{(4)}](t) = \\ &= G_h^{(\ell)}[f^{(1)},f^{(2)},f^{(3)},f^{(4)}](t) - L_h^{(\ell)}[f^{(1)},f^{(2)},f^{(3)},f^{(4)}](t) \quad (\ell = 1, 2, 3, 4), \end{aligned} \tag{3}$$

and

$$\begin{aligned} G_h^{(\ell)}[f^{(1)},f^{(2)},f^{(3)},f^{(4)}](t) &= \sum_{i,j}^{1\ldots m_\ell} \tau_{ij}^{\ell} F^h{}_{ij}(\ell) f_i^{(\ell)}(t) f_j^{(\ell)}(t) + \\ &\quad + \sum_{k \neq \ell}^{1\ldots 4} \sum_{i=1}^{m_\ell} \sum_{j=1}^{m_k} \eta_{ij}^{\ell k} \Phi^h{}_{ij}(\ell, k) f_i^{(\ell)}(t) f_j^{(k)}(t), \\ L_h^{(\ell)}[f^{(1)},f^{(2)},f^{(3)},f^{(4)}](t) &= f_h^{(\ell)}(t) \left[\sum_{i,j}^{1\ldots m_\ell} \tau_{hj}^{\ell} F_{hj}^{i}(\ell) f_j^{(\ell)}(t) + , \right. \\ &\quad \left. + \sum_{k \neq \ell}^{1\ldots 4} \sum_{i=1}^{m_\ell} \sum_{j=1}^{m_k} \eta_{hj}^{\ell k} \Phi_{hj}^{i}(\ell, k) f_j^{(k)}(t) \right] \end{aligned} \tag{4}$$

For obvious reasons, the term $G_h^{(\ell)}[f^{(1)},f^{(2)},f^{(3)},f^{(4)}](t)$ is called *gain term*, while the term $L_h^{(\ell)}[f^{(1)},f^{(2)},f^{(3)},f^{(4)}](t)$ is called *loss term*. For the sake of clarity, we explicitly note that system (2) consists of $m = m_1 + m_2 + m_3 + m_4$ equations

The *Cauchy problem* associated with system (1) is obtained by adding to Equation 1 the *initial conditions*

$$f_h^{(\ell)}(0) = f_{h,0}^{(\ell)}, \quad \forall \ \ell \in \{1, 2, 3, 4\}, \ \forall \ h \in \{1, 2, \ldots, m_\ell\}, \tag{5}$$

3 | THE MODEL FOR COVID EPIDEMICS

This Section is devoted to apply the general model scheme sketched in the previous one to the description and prediction not only of the evolution of an epidemic but also of the pressure it exerts on the care structures, with a special concern to COVID epidemic at present afflicting almost the whole world and in particular to a comparison between the effects on its

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[*] From now on to the end of the paper, each system of equations will be identified by a single numerical label and each of the equations that compose it will be distinguished by a subscript corresponding to its position in the system: for instance, the third equation of system (X) will be indicated as $(X)_3$.

evolution of different "degrees" of containment measures (lockdowns), to establish—in view of the evident widespread and heavy consequences of lockdown—the effectiveness of lockdown strategy.

Accordingly, all the variables introduced in the previous Section will be given the following interpretation:

1. S is of course the whole system of individuals and *resources* of a national population, in which we consider *four* functional subsystems: (a) S_1 will denote the subsystem of single human individuals, that is, the elements of S who can be hit by the virus or not; (b) the «particles» of S_h, for any $h = 2, 3, 4$, are «care structures», that are to be meant as systems consisting of a physician (who will be in general the same for several structures, but this is quite irrelevant in our scheme), and of a place of care (home, a room in a hotel, a bed in a hospital) and of a number of care tools and drugs. More precisely, (c) S_2 will be the subsystem of lowest-level care structures (just a place to rest—mainly *not* in a hospital—and drugs, with or without the help of a physician); (d) S_3 will be the subsystem of medium-level care structures (a place to rest—mainly in a hospital—and drugs and oxygen tanks); (e) S_4 will be the subsystem of high-level care structures (intensive care);
2. the variable u_1, which in the sequel will be simply denoted by the symbol u, is the «health state» and can take six values, that is, $D_1 \equiv \{0, 1, 2, 3, 4, 5\}$, where 0 = *healthy*, 1 = *asymptomatic*, 2 = *mild symptoms*, 3 = *acute symptoms*, 4 = *severe symptoms*, 5 = *death*;
3. the variables u_2, u_3, u_4 are all the same variable v, which will be called the «efficiency» and will be given three values, that is, $D_2 = D_3 = D_4 = \{0, 1, 2\}$, where 0 = *exhausted*, 1 = *low efficiency*, 2 = *full efficiency*.

In connection with the above definitions and the choice of the range of values for both the variables introduced above, it could be worth noting that, while the six levels chosen for the state variable u seem to be quite natural, the choice to assign only three values to the state variable v is simply due to the aim to find a reasonable compromise between producing a sufficiently accurate picture of the problem and managing a reasonably low number of equations when performing numerical simulations.

It is also necessary to point out that the choice to consider *death* among the values of the health state variable u must be thought of as alternative to the need of tackling the formal complication related to managing a system with a variable number of members. In this connection, it should be carefully noted that, at least in the discrete homogeneous case, the explicit consideration of an «out» state value could result in a remarkable technical improvement of the analysis of this case. And, of course, this consideration could be also «exported» to the continuous case by using vector state variables.[35-37] On the other hand, the explicit consideration of an «absorbing» state is well-known and frequently used in the study of stochastic processes.

This stated, we must turn our attention to the values of the «parameters» of the population, that regulate the evolution of the distributions of u and v, that is, the coefficients of Equation 2, appearing in relations (3) and (4).

To start with, let us consider the encounter rates and, among them, τ^2_{ij} τ^3_{ij} and τ^4_{ij} first. Since no care structure interacts with other care structures, if not in the sense that one of them passes some patients to another at a different level (which only modifies the interaction rates between sick individuals and care structures), we feel allowed to set $\tau^2_{ij} = \tau^3_{ij} = \tau^4_{ij} = 0$ for any i and j in $\{0, 1, 2\}$. For the same reason, we should also set $\eta^{23}_{ij} = \eta^{32}_{ij} = \eta^{24}_{ij} = \eta^{42}_{ij} = \eta^{34}_{ij} = \eta^{43}_{ij} = 0$ for any i and j in $\{0, 1, 2\}$.

The encounter rates τ^1_{ij} and η^{1k}_{ij}, $\eta^{\ell 1}_{ij}$ need a somehow deeper discussion. Starting with the latter ones, we must observe that η^{1k}_{ij} should give the average number per unit time of individuals in the health state i receiving some kth level care from a structure in an efficiency state j. Accordingly, $\eta^{1k}_{0j} = 0$ and $\eta^{1k}_{1j} = \eta^{1k}_{5j} = 0$ for any $k = 2, 3, 4$ and any $j = 0, 1, 2$. Furthermore, it is quite natural to assume that any individual of health state k will be taken in charge only by a kth level care structure, that is, that $\eta^{13}_{2j} = \eta^{14}_{2j} = \eta^{14}_{3j} = 0$, for any j. In other words, the only encounter rates η^{1k}_{kj} are different from zero. And, for obvious reasons of symmetry, $\eta^{k1}_{0j} = 0$ and $\eta^{k1}_{1j} = \eta^{k1}_{5j} = 0$ for any $k = 2, 3, 4$ and any $j = 0, 1, 2$, $\eta^{31}_{2j} = \eta^{31}_{4j} = \eta^{41}_{2j} = \eta^{41}_{3j} = 0$, for any j, so that the only encounter rates η^{k1}_{ik} are different from zero.

Now, what should we state about nonzero encounter rates? Consider any parameter η^{1k}_{kj}, and observe that all individuals of S in the health state k in a given unit time will be taken care of in some care structures of kth level (conventionally, the individuals who cannot find any efficient care structure where they could get help, «interact» with exhausted structures). Moreover, the fraction of individuals interacting with structures of any state depends on the distribution of states over the class of structures. As a consequence, we can write

$$\sum_{j=0}^{2} \eta^{1k}_{kj} f^{(k)}_j = 1.$$

that is, *provided* we experience an individual in the health state k, there will be a kth level care structure (possibly exhausted) which will interact with it. On the other hand, there is no reason why the encounter rate should take different values for different conditions of the care structure, as each infected individual aims to be taken in charge by a structure at the highest efficiency level, and his possible «transition» from a structure at level h to a structure at level $h-1$ or at level $h-2$ is a consequence of his interaction as well as of newly added interactions.

An analogous reasoning must be carried out about the encounter rates τ^1_{ij} (with $i,j = 0,1,2,3,4,5$), keeping in mind that, in connection with infection, interactions are simply physical contacts or excessive physical nearness. Therefore, we can assume that $\tau^1_{03} = \tau^1_{30} = \tau^1_{04} = \tau^1_{40} = \tau^1_{05} = \tau^1_{50} = \tau^1_{13} = \tau^1_{31} = \tau^1_{14} = \tau^1_{41} = \tau^1_{15} = \tau^1_{51} = \tau^1_{23} = \tau^1_{32} = \tau^1_{24} = \tau^1_{42} = \tau^1_{25} = \tau^1_{52} = \tau^1_{34} = \tau^1_{43} = \tau^1_{35} = \tau^1_{53} = \tau^1_{45} = \tau^1_{54} = 0$, This corresponds to assuming that hospitalized (and, of course, dead) people (at health sates 2, 3, 4, and 5) cannot interact with each other nor with susceptible people (walking people, at health states 0 and 1).

Now, the remaining encounter rates (τ^1_{ij} with $(i,j) \in \{0,1\}^2$ and η^{1k}_{kr} and η^{k1}_{kr} with $k \in \{2,3,4\}$ and $r \in \{0,1,2\}$, as expected numbers of interactions per unit time, should be estimated in dependence on some official statistical information about the daily behavior of the members of the population under examination, but such an information is not available. So, this article could not but adopt the converse method of assigning to them arbitrary values, which could be modified *a posteriori* by comparing the results given here with the empirical curves drawn from official data. On the other hand, since the present analysis is mainly devoted to compare different predicted evolutions of Covid-19 disease with and without containment measures (total or partial «lockdown»), the actual values of the encounter rates under different conditions are much less important than their ratios. So, we feel allowed to assume that all the encounter rates τ^1_{ij} $(i,j \in \{0,1,2\})$ are constant with respect to time (at least for small time intervals) and all equal to each other, and denote by τ their common value. In particular, we set $\tau = 50$ in the absence of any lockdown, and since we aim to carry out our analysis for the case of Italian population, we consider three different values of τ for partial and total lockdown, namely (a) $\tau = 10$ (partial lockdown in «yellow zones»), (b) $\tau = 5$ (partial lockdown in «orange zones»), and (c) $\tau = 2.5$ (total lockdown in «red zones»). All these encounter rates, with the only possible exception of the last one, are probably rather overestimated, but, if so, such an overestimation would simply result in an underestimation of the effectiveness of lockdown, which seems to be a prudential «bias» on the result. A more careful discussion of this point will be offered in the last section of this article.

In the same line of thought, the encounter rates η^{1k}_{kr} and η^{k1}_{kr} will be also given arbitrary values. In particular, they must be obtained as averages of the official data of Campania region in Italy during the so-called «second wave» of infection in the last four months.

This stated, what is left to do is to assign the transition matrices. We list them below, with only few comments.

First of all, $F^r{}_{s0}(1) = \delta^r_s$, for $0 \le r \le 5, 0 \le s \le 5$, where $\delta^r_s = 0$ if $r \ne s$ and $\delta^r_s = 1$ if $r = s$. Next, setting

$$\mathbf{F}_{,i}(1) = \begin{pmatrix} F^0{}_{0i}(1) & F^1{}_{0i}(1) & F^2{}_{0i}(1) & F^3{}_{0i}(1) & F^4{}_{0i}(1) & F^5{}_{0i}(1) \\ F^0{}_{1i}(1) & F^1{}_{1i}(1) & F^2{}_{1i}(1) & F^3{}_{1i}(1) & F^4{}_{1i}(1) & F^5{}_{1i}(1) \\ F^0{}_{2i}(1) & F^1{}_{2i}(1) & F^2{}_{2i}(1) & F^3{}_{2i}(1) & F^4{}_{2i}(1) & F^5{}_{2i}(1) \\ F^0{}_{3i}(1) & F^1{}_{3i}(1) & F^2{}_{3i}(1) & F^3{}_{3i}(1) & F^4{}_{3i}(1) & F^5{}_{3i}(1) \\ F^0{}_{4i}(1) & F^1{}_{4i}(1) & F^2{}_{4i}(1) & F^3{}_{4i}(1) & F^4{}_{4i}(1) & F^5{}_{4i}(1) \\ F^0{}_{5i}(1) & F^1{}_{5i}(1) & F^2{}_{5i}(1) & F^3{}_{5i}(1) & F^4{}_{5i}(1) & F^5{}_{5i}(1) \end{pmatrix}, \tag{6}$$

we have

$$\mathbf{F}_{,1}(1) = \begin{pmatrix} 0.05 & 0.76 & 0.0855 & 0.0665 & 0.038 & 0 \\ 0 & 1 & 0 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 0 & 0 & 1 \end{pmatrix}, \tag{7}$$

$$\mathbf{F}_{,2}(1) = \begin{pmatrix} 0.05 & 0.76 & 0.0855 & 0.0665 & 0.038 & 0 \\ 0 & 1 & 0 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 0 & 0 & 1 \end{pmatrix}. \tag{8}$$

It must be carefully noted that the probabilities given in the first rows of the above matrices simply express that the probability that an healthy (but *susceptible*, as we in principle consider *all* the members of the population) individual be infected as a consequence of an interaction with an infected individual is 95%. This probability is estimated according to recent results about Covid-19, which seem to show that interaction does not necessarily imply infection. It could be objected that this probability is somehow underestimated: but, on one hand, our present knowledge of the transmission of Covid-19 does not allow a more precise estimate, and, on the other hand, this will not substantially affect the comparison of the solutions with different degrees of containment measures.

Finally, we have completely disregarded the matrices $\mathbf{F}_{,i}(1)$ with $i \in \{3, 4, 5\}$ and the matrices $\mathbf{F}_{,i}(h)$ for $h \in \{2, 3, 4\}$ and $i \in \{0, 1, 2\}$ in view of our assumptions on encounter rates τ_{ij} for any i and any $j \in \{3, 4, 5\}$ and on the absence of interactions between care structures, bearing in mind that no interaction implies no change of state.

Now, we set

$$\mathbf{\Phi}_{,j}(1,k) = \begin{pmatrix} \Phi^0{}_{0j}(1,k) & \Phi^1{}_{0j}(1,k) & \Phi^2{}_{0j}(1,k) & \Phi^3{}_{0j}(1,k) & \Phi^4{}_{0j}(1,k) & \Phi^5{}_{0j}(1,k) \\ \Phi^0{}_{1j}(1,k) & \Phi^1{}_{1j}(1,k) & \Phi^2{}_{1j}(1,k) & \Phi^3{}_{1j}(1,k) & \Phi^4{}_{1j}(1,k) & \Phi^5{}_{1j}(1,k) \\ \Phi^0{}_{2j}(1,k) & \Phi^1{}_{2j}(1,k) & \Phi^2{}_{2j}(1,k) & \Phi^3{}_{2j}(1,k) & \Phi^4{}_{2j}(1,k) & \Phi^5{}_{2j}(1,k) \\ \Phi^0{}_{3j}(1,k) & \Phi^1{}_{3j}(1,k) & \Phi^2{}_{3j}(1,k) & \Phi^3{}_{3j}(1,k) & \Phi^4{}_{3j}(1,k) & \Phi^5{}_{3j}(1,k) \\ \Phi^0{}_{4j}(1,k) & \Phi^1{}_{4j}(1,k) & \Phi^2{}_{4j}(1,k) & \Phi^3{}_{4j}(1,k) & \Phi^4{}_{4j}(1,k) & \Phi^5{}_{4j}(1,k) \\ \Phi^0{}_{5j}(1,k) & \Phi^1{}_{5j}(1,k) & \Phi^2{}_{5j}(1,k) & \Phi^3{}_{5j}(1,k) & \Phi^4{}_{5j}(1,k) & \Phi^5{}_{5j}(1,k) \end{pmatrix}, \tag{9}$$

for $k = 2, 3, 4$ and $j = 0, 1, 2$ and

$$\mathbf{\Phi}_{,j}(2,1) = \begin{pmatrix} \Phi^0{}_{0j}(2,1) & \Phi^1{}_{0j}(2,1) & \Phi^2{}_{0j}(2,1) \\ \Phi^0{}_{1j}(2,1) & \Phi^1{}_{1j}(2,1) & \Phi^2{}_{1j}(2,1) \\ \Phi^0{}_{2j}(2,1) & \Phi^1{}_{2j}(2,1) & \Phi^2{}_{2j}(2,1) \end{pmatrix}, \tag{10}$$

for $2 = 2, 3, 4$ and $j = 0, 1, 2, 3, 4, 5$. We assume

$$\mathbf{\Phi}_{,0}(1,2) = \begin{pmatrix} 1 & 0 & 0 & 0 & 0 & 0 \\ 1 & 0 & 0 & 0 & 0 & 0 \\ 0.1 & 0 & 0.4 & 0.5 & 0 & 0 \\ 0 & 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 0 & 0 & 1 \\ 0 & 0 & 0 & 0 & 0 & 1 \end{pmatrix}, \tag{11}$$

$$\mathbf{\Phi}_{,1}(1,2) = \begin{pmatrix} 1 & 0 & 0 & 0 & 0 & 0 \\ 1 & 0 & 0 & 0 & 0 & 0 \\ 0.4 & 0 & 0.3 & 0.3. & 0 & 0 \\ 0 & 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 0 & 0 & 1 \\ 0 & 0 & 0 & 0 & 0 & 1 \end{pmatrix}, \tag{12}$$

$$\mathbf{\Phi}_{,2}(1,2) = \begin{pmatrix} 1 & 0 & 0 & 0 & 0 & 0 \\ 1 & 0 & 0 & 0 & 0 & 0 \\ 0.7 & 0 & 0.2 & 0.1 & 0 & 0 \\ 0 & 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 0 & 0 & 1 \\ 0 & 0 & 0 & 0 & 0 & 1 \end{pmatrix}, \tag{13}$$

$$\mathbf{\Phi}_{,0}(1,3) = \begin{pmatrix} 1 & 0 & 0 & 0 & 0 & 0 \\ 1 & 0 & 0 & 0 & 0 & 0 \\ 1 & 0 & 0 & 0. & 0 & 0 \\ 0 & 0 & 0.1 & 0.1 & 0.8 & 0 \\ 0 & 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 0 & 0 & 1 \end{pmatrix}, \tag{14}$$

$$\mathbf{\Phi}_{,1}(1,3) = \begin{pmatrix} 1 & 0 & 0 & 0 & 0 & 0 \\ 1 & 0 & 0 & 0 & 0 & 0 \\ 1 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0.3 & 0.2 & 0.5 & 0 \\ 0 & 0 & 0 & 0 & 0 & 1 \\ 0 & 0 & 0 & 0 & 0 & 1 \end{pmatrix}, \tag{15}$$

$$\mathbf{\Phi}_{,2}(1,3) = \begin{pmatrix} 1 & 0 & 0 & 0 & 0 & 0 \\ 1 & 0 & 0 & 0 & 0 & 0 \\ 1 & 0. & 0 & 0 & 0 & 0 \\ 0 & 0 & 0.7 & 0.1 & 0.2 & 0 \\ 0 & 0 & 0 & 0 & 0 & 1 \\ 0 & 0 & 0 & 0 & 0 & 1 \end{pmatrix}, \tag{16}$$

$$\mathbf{\Phi}_{,0}(1,4) = \begin{pmatrix} 1 & 0 & 0 & 0 & 0 & 0 \\ 1 & 0 & 0 & 0 & 0 & 0 \\ 1 & 0 & 0 & 0 & 0 & 0 \\ 1 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0.2 & 0 & 0.8 \\ 0 & 0 & 0 & 0 & 0 & 1 \end{pmatrix}, \tag{17}$$

$$\mathbf{\Phi}_{,1}(1,4) = \begin{pmatrix} 1 & 0 & 0 & 0 & 0 & 0 \\ 1 & 0 & 0 & 0 & 0 & 0 \\ 1 & 0 & 0 & 0 & 0 & 0 \\ 1 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0.5 & 0 & 0.5 \\ 0 & 0 & 0 & 0 & 0 & 1 \end{pmatrix}, \tag{18}$$

$$\mathbf{\Phi}_{,2}(1,4) = \begin{pmatrix} 1 & 0 & 0 & 0 & 0 & 0 \\ 1 & 0 & 0 & 0 & 0 & 0 \\ 1 & 0 & 0 & 0. & 0 & 0 \\ 1 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0.8 & 0 & 0.2 \\ 0 & 0 & 0 & 0 & 0 & 1 \end{pmatrix}, \tag{19}$$

while, as far as the transition probabilities between the efficiency states of care structures, we shall consider *two* different systems of assumptions, whose influences on the solutions of the system of equations obtained when the numerical values are inserted in system (1) will be compared in the simulations proposed in our next paper addressed to the analysis of epidemics. The first set of values is given by the following matrices:

$$\mathbf{\Phi}_{,2}(2,1) = \mathbf{\Phi}_{,3}(3,1) = \mathbf{\Phi}_{,4}(4,1) = \begin{pmatrix} 1 & 0 & 0 \\ 0.6 & 0.4 & 0 \\ 0 & 0.6 & 0.4 \end{pmatrix}, \tag{20}$$

while the second set is shown below:

$$\mathbf{\Phi}_{,2}(2,1) = \mathbf{\Phi}_{,3}(3,1) = \mathbf{\Phi}_{,4}(4,1) = \begin{pmatrix} 1 & 0 & 0 \\ 0.1 & 0.9 & 0 \\ 0 & 0.1 & 0.9 \end{pmatrix}, \tag{21}$$

Now, the conditional probabilities in the above matrices require at least some comments. First of all, most of them have been introduced for completeness and have been given arbitrary values, as they correspond to interactions that have no place and, as a consequence, they are—strictly speaking—undefined. The remaining ones should have been estimated as suitable averages of the official data furnished by institutions about the ratios of the number of deaths and of the number of healed people to the number of infected people in at least one selected region. But the official data actually available are quite insufficient to obtain a single set of estimates. So, we have chosen to formulate a set of arbitrary assumptions, and to adopt a «random walk» scheme. It should also be noted that the «negative» probabilities, that is, the probabilities of moving from a state i to a state $j > i$ are systematically overestimated. In view of our aim to deduce a mathematical comparison of the evolutions of the pandemics with and without containment measures, this choice seems to be the most prudential one.

This stated, with the above chosen values for the encounter rates and the transition probabilities, we obtain the following system of 15 nonlinear ordinary differential equations in 15 unknown probability distribution functions (where, for the sake of a better readability, we have chosen to set $f^{(1)} = X, f^{(2)} = Y, f^{(3)} = Z, f^{(4)} = U$):

$$\begin{aligned}
\frac{\mathrm{d}X_0}{\mathrm{d}t}(t) = {} & -0.95\tau X_0(t)[X_1(t) + X_2(t)] + \\
& + \tau X_2(t)[0.1Y_0(t) + 0.4Y_1(t) + 0.7Y_2(t)] + 92X_1(t), \\
\frac{\mathrm{d}X_1}{\mathrm{d}t}(t) = {} & \tau X_0(t)[0.76X_1(t) + 0.76X_2(t) + X_1(t)] + \\
& - \tau X_1(t)[2X_0(t) + X_1(t) + X_2(t)] - 92X_1(t), \\
\frac{\mathrm{d}X_2}{\mathrm{d}t}(t) = {} & 0.0855\tau X_0(t)[X_1(t) + X_2(t)] + \\
& + 100X_2(t)[0.2Y_2(t) - 0.1Y_0(t) - 0.5Y_0(t) - 0.4Y_1(t) - 0.7Y_2(t) - 0.1Y_2(t)] + \\
& + 0.1 \cdot 100X_3(t)Z_0(t) + 0.3 \cdot 100X_3(t)Z_1(t) + 0.7 \cdot 100X_3(t)Z_2(t), \\
\frac{\mathrm{d}X_3}{\mathrm{d}t}(t) = {} & 0.0665\tau X_0(t)[X_1(t) + X_2(t)] + 100X_2(t)[0.5Y_0(t) + 0.3Y_1(t) + 0.1Y_2(t)] + \\
& + 16X_4(t)[0.2U_0(t) + 0.5U_1(t) + 0.8U_2(t)] + \\
& - [0.1 \cdot 100X_3(t)Z_0(t) + 0.3 \cdot 100X_3(t)Z_1(t) + 0.7 \cdot 100X_3(t)Z_2(t) + \\
& + 0.8 \cdot 100X_3(t)Z_0(t) + 0.5 \cdot 100X_3(t)Z_1(t) + 100X_3(t)Z_2(t)], \\
\frac{\mathrm{d}X_4}{\mathrm{d}t}(t) = {} & 0.038\tau X_0(t)X_1(t) + 0.038\tau X_0(t)X_2(t) + \\
& + 0.8 \cdot 100X_3(t)Z_0(t) + 0.5 \cdot 100X_3(t)Z_1(t) + 0.2 \cdot 100X_3(t)Z_2(t) + \\
& - 0.2 \cdot 16X_4(t)U_0(t) - 0.8 \cdot 16X_4(t)U_0(t) - 0.5 \cdot 16X_4(t)U_1(t) + \\
& - 0.8 \cdot 16X_4(t)U_2(t) - 0.2 \cdot 16X_4(t)U_2(t),
\end{aligned}$$

$$\frac{\mathrm{d}X_5}{\mathrm{d}t}(t) = 0.8 \cdot 16X_4(t)U_0(t) + 0.5 \cdot 16X_4(t)U_1(t) + 0.2 \cdot 16X_4(t)U_2(t),$$

$$\frac{\mathrm{d}Y_0}{\mathrm{d}t}(t) = 100\Phi^0_{1,2}(2,1)Y_1(t)X_2(t), \tag{22}$$

$$\begin{aligned}
\frac{\mathrm{d}Y_1}{\mathrm{d}t}(t) &= 100\Phi^1_{2,2}(2,1)Y_2(t)X_2(t) - 100\Phi^0_{1,2}(2,1)Y_1(t)X_2(t),\\
\frac{\mathrm{d}Y_2}{\mathrm{d}t}(t) &= -100\Phi^1_{2,2}(2,1)Y_2(t)X_2(t),\\
\frac{\mathrm{d}Z_0}{\mathrm{d}t}(t) &= 100\Phi^0_{1,3}(3,1)Z_1(t)X_3(t),\\
\frac{\mathrm{d}Z_1}{\mathrm{d}t}(t) &= 100\Phi^1_{2,2}(2,1)Z_2(t)X_3(t) - 100\Phi^0_{1,2}(3,1)Z_1(t)X_3(t),\\
\frac{\mathrm{d}Z_2}{\mathrm{d}t}(t) &= -100\Phi^1_{2,3}(3,1)Z_2(t)X_3(t),\\
\frac{\mathrm{d}U_0}{\mathrm{d}t}(t) &= 16\Phi^0_{1,4}(4,1)U_1(t)X_4(t),\\
\frac{\mathrm{d}U_1}{\mathrm{d}t}(t) &= 16\Phi^1_{2,4}(4,1)U_2(t)X_4(t) - 16\Phi^0_{1,4}(4,1)U_1(t)X_4(t),\\
\frac{\mathrm{d}U_2}{\mathrm{d}t}(t) &= -16\Phi^1_{2,4}(4,1)U_2(t)X_4(t),
\end{aligned}$$

where, as laid out above, the transition probabilities in the last nine equations, depending on the tools and the staff provided to the care structures, as well the encounter rates between the members of the population, have been left unspecified, since they can take different systems of values that will be used in a forthcoming paper to compare the different situations to which they correspond.

Finally, special attention must be paid to the additional term $92X_1$ appearing in Equation 22_1 as a gain term and in Equation 22_2 as a loss term. This term, which does not appear in the abstract formulation of system (1), corresponds to the natural healing process which «displaces» individuals from the asymptomatic state 1 to the healthy state 0. Its absence in the system of Equation 1 is evidently due to the basic theoretical assumption that state changes in any complex system whose behavior must be described by a KTAP model can occur only as consequences of interactions. This assumption is a form of «inertia principle» and the context of epidemics shows that it cannot be accepted for all systems. This point is discussed in a paper in preparation.[48] The coefficient 92 is obtained as the product of healing probability of an asymptomatic individual (= 1) times the number of asymptomatic individuals who in a unit time result to have recovered their health. This number has been obtained by averaging over the whole period the number of asymptomatic individuals officially recorded each day in Campania region, considering 15 days the time required to go back to the state 0 and choosing one day as time unit. The «mixed» encounter rates $\eta^{1k}_{kj} = \eta^{k1}_{jk} = \eta_k$, on the other hand, have been estimated as percentages of suitable averages of the data about hospitalized (requiring and not requiring intensive care) people in the same region.

4 | CONCLUSIONS AND PERSPECTIVES

The system of Equation 22 has been obtained from the general system of KTAP by means of a suitable specializations of the parameters that rule the interactions between the «active particles» of the complex systems to which it applies, as well as their consequences. It is almost impossible to overestimate the relevance of these parameters and their influence on the solutions: for this reason, the study of continuous dependence of solutions on the values of encounter rates and transition probabilities, started in Reference 47, as well as of the possible emergence of instability effects, needs to be (and will be in fact) continued in future research. On the other hand, in view of future applications, sampling and estimating such parameters as the encounter rates and the transition probabilities should become an habit in appropriate institutions and laboratories. Unfortunately, because of the extremely large size of the involved populations, the estimation of parameters seems to be an almost impossible task to be faced, and the most effective way to follow in order to obtain mathematical portraits sufficiently faithful to reality will be to assign arbitrarily many different systems of parameters, then to simulate the solutions corresponding to the assigned values and finally to compare them with experimental evidence. In case of disagreement, the model should be applied with a different choice of parameters, and the simulated solution corresponding to this new choice should be compared again with the experimental evidence, and these steps should be repeated several times to correct the values of parameters. This procedure, which is indeed rather complicated and would probably require the use of tools of parallel calculus, would however allow to estimate the actual values of parameters *a posteriori*. A first step in this direction will consist in the simulations of solutions to system (22). As repeatedly laid out in the Introduction, these simulations could not be presented here, and will be carried out in future papers, also in order to enlighten the above outlined «tuning» procedure for parameters.

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