Epidemics and Local Demographic Dynamics

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Abstract

The investigation of the interactions between the demographic dynamics of a healthy population and the perturbations induced in it by the progession of an epidemics is the object of this study. A SIR epidemic model is progressively enriched with demographic features, such as birth-death imbalance, disease-induced deaths, vertical transmission and infectious immigration and its equilibria are investigated. A statistical setting is then established in order to test the relevance of the demographic features of the various modelling hypotheses.

Key Words: demographic dynamics, epidemic model, basic reproduction number, immigration, vertical transmission, disease-free equilibrium, estimation, hypothesis testing.

1. Introduction

The relationship between the local (or natural) demographic dynamics and the dynamics of infectious diseases is one of the relevant aspects of the epidemic process that is sometimes neglected in mathematical models. Often, a healthy population at demographic equilibrium, sometimes supplemented with vertical transmission, or, at most, an "*a posteriori*" variable total population (in the sense of a population at disease-

induced imbalance) is what is used in epidemic modelling and most of the attention is focussed on the understanding of the susceptible-infective dynamics. However, as shown in a few existing studies, the interaction between epidemiological indicators and demographic dynamics is sometimes an imprescindable aspect of epidemics: this is particularly evident in the light of the alarming course taken by such infections as HIV/AIDS, malaria, tuberculosis and others, which have proved to be able to affect the demographic balance of whole nations and even continents. The globalization of human contacts and the migration flows also play a relevant role in the transformations of the epidemic processes, but their inclusion in the models is still rather limited to special cases, while even important studies still omit them.

In its first part, this paper presents a classification of various demographic features and their interactions with the infection dynamics, also in view of applications to global epidemics and epidemics in developping countries (imbalanced populations with high birth and mortality rates and relatively isolated communities). Various demographic and disease-related features (balanced to imbalanced population, vertical transmission, immigration) are progressively added to a mass action incidence SIR model (susceptible, infective and removed individuals with proportional force-of-infection) and equilibria are determined and analyzed in terms of basic reproduction number and of natural demography parameters. Simulations are also used to point out the differences between the models here presented in terms of graphical representations.

The second part of the paper proposes a novel statistical procedure of hypothesis testing to ascertain the specificity of the population under study and the model to be applied in the study of the epidemics.

2. Classification of Models

The SIR structure of epidemic models, with demographic dynamics, is used to describe several infections, whose specific feature is the acquisition of a permanent immunity upon recovery from the disease. However, the structure is flexible enough to accommodate partially or completely fatal diseases, vertical transmission and demographic imbalance due to either natural demographic dynamics or to disease-induced mortality or reduction of fertility. All these aspects are considered in the following listing and classification of SIR models: a hyerarchical order is followed in the progressive introduction of features into the basic structure of model 1. and the system of differential equations describing the mathematical structure, a schematic analysis of the steady state conditions and a graphic compartmental representation are provided for each of the six models considered.

2.1 *Models with balanced population*

When an infection invades a healthy population, there are only two possible initial demographic situations: either the population is at equilibrium, as in “mature” societies, like many western Europeans countries, or there exists an imbalance between births and deaths, as in most developping countries, where, for sociological and economic reasons, the birth rate is always higher than the death rate. The infection splits the population into categories classified according to their contact with the infectious agent: if the

infection is relevant enough to alter the biological/clinical status of the infected individual, then each of the category may present modifications of its vital dynamics such as disease-induced extra mortality during infection and a reduction of fertility or infertility during and/or after infection. This first category of models, presents a population at equilibrium invaded by disease which is non-fatal in the first model (no modifications of the demographic dynamics observed) and fatal in the second one (disease-induced extra mortality for the category of infective individuals).

Model 1: Non-fatal Disease Model

When the disease does not causes death and the birth rate μ equals the death rate, then the total population remains stable at the disease-free level *N*.

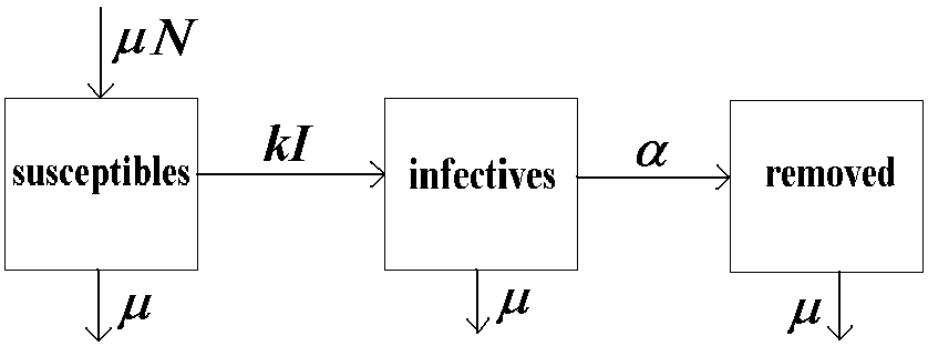

Figure 1: SIR model with disease-free population at equilibrium

The model is described by the following system of ODE's:

$$\begin{cases} \dfrac{dS(t)}{dt} = \mu N - kS(t)I(t) - \mu S(t) \\ \dfrac{dI(t)}{dt} = kS(t)I(t) - (\mu + \alpha)I(t) \\ \dfrac{dR(t)}{dt} = aI(t) - \mu R(t) \end{cases} \tag{1}$$

whose steady states are given by a disease-free equilibrium $\left(\bar{S} = N; \bar{I} = 0\right)$ and an endemic equilibrium:

$$\begin{cases} \bar{S} = \dfrac{\mu + \alpha}{k} \\ \bar{I} = \dfrac{\mu N}{\mu + \alpha}\left(1 - \dfrac{1}{R_0}\right) \end{cases} \tag{2}$$

where the basic reproduction number is given by $R_0 = \dfrac{kN}{\mu + a}$ and presents a bifurcation between the two steady states at $R_0 = 1$.

By dividing the model variables by the total population $s = \dfrac{S}{N}$, $i = \dfrac{I}{N}$ and multiplying each parameter by the mean duration of infection $(\mu + \alpha)^{-1}$ the following non-dimensional endemic equilibrium is obtained:

$$\begin{cases} \bar{s} = \dfrac{1}{R_0} \\ \bar{i} = m\left(1 - \dfrac{1}{R_0}\right) \end{cases} \tag{3}$$

Model 2: Fatal Disease Model

When the severity of the disease is such that a substantial portion ξ of the infectives dies because of the clinical consequencies of the disease, then the total population $N(t) = S(t) + I(t) + R(t)$ is subject to disease-induced variability and the model is described by the following ODE's system:

$$\begin{cases} \dfrac{dS(t)}{dt} = \mu\big(S(t) + I(t) + R(t)\big) - kS(t)I(t) - \mu S(t) \\ \dfrac{dI(t)}{dt} = kS(t)I(t) - (\mu + \xi + \alpha)I(t) \\ \dfrac{dR(t)}{dt} = aI(t) - \mu R(t) \end{cases} \tag{4}$$

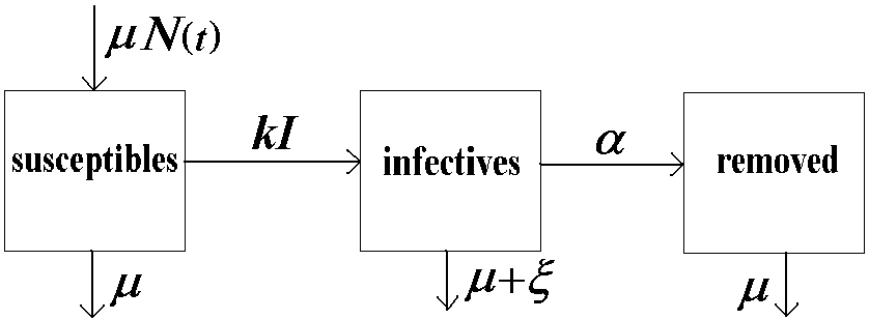

Figure 2: SIR model with disease-free population at equilibrium and disease-induced deaths.

By using the balance equation for the total population we have

$$\frac{dN(t)}{dt} = \frac{dS(t)}{dt} + \frac{dI(t)}{dt} + \frac{dR(t)}{dt} = -\xi I(t) \tag{4.1}$$

which indicates that the total population experiences a phase of decrease until extinction or until the disease is eradicated (i.e., $N'(t) < 0 \ \ \forall t \le \tau$ where $\tau = \inf\{t : I(t) = 0\}$): in this latter case, the population recovers constancy after the disease eradication. Therefore, the only admissible equilibrium of (4) is given by the disease-free state $(\overline{S};0)$ attained after the disease eradication; the total number of remaining individuals stabilizes at an equilibrium level $\overline{S}$, obviously lower than the initial population size $N(0)$ because of the effects of the infection outbreaks. It is then important to detect the new population size $\overline{S}$ on the basis of the epidemic dynamics expressed by (4): if the initial population size is large enough and the virulence of the infection is not too strong, then the epidemic may be eradicated before the complete extinction of the population. By integrating both sides of (4.1) and by recalling the non-increasingness of $N(t)$ and its definition, we have

$$N(0) > N(t) = -\xi \int_0^t I(y)dy + N(0) = S(t) + I(t) + R(t)$$

and by assuming that $\lim_{t\to\infty} N(t) > 0$ and $\lim_{t\to\infty} I(t) = 0$ (and, therefore, $R(t) \underset{t\to\infty}{\to} 0$), the final population size is given by

$$\overline{S} = \lim_{t\to\infty} S(t) = -\xi \lim_{t\to\infty} \int_0^t I(y)dy + N(0)$$

where $N(0) > \bar{S} > 0$.

Since the total population is destined to extinction at some time t' if the number of infectives does not vanish before, then the basic reproduction number $R_0 = \frac{kN(0)}{\mu + \xi + \alpha}$ (i.e., the number of new infections caused by an infectious individual in an infection-free population) identifies the mode of approach to the disease-free equilibrium.

It is clear that, given the disease-free equilibrium of the population, only the presence of infectives can alter such equilibrium and, therefore, reduce the total size of the population: this depletion only occurs during the epidemic outbreaks and disappears when the infection is eradicated from the population. If $N(0) > \xi \lim_{t\to\infty} \int_0^t I(y)dy$ then the outbreak leaves a surviving population of size $0 < \bar{S} < N(0)$, otherwise the disease causes the extinction of the population.

Two equilibria of the system are detected: the disease-free equilibrium $\left(\bar{S} = \bar{N}; \bar{I} = 0\right)$ refers to a total equilibrium population equal to the initial value $S(0)$; the endemic equilibrium is given by

$$\begin{cases} \bar{S} = \dfrac{\mu + \xi + \alpha}{k} \\ \bar{I} = \dfrac{\mu \bar{N}}{\mu + \xi + \alpha}\left(1 - \dfrac{1}{R_0}\right) \end{cases} \tag{5}$$

where the basic reproduction number $R_0 = \dfrac{k\overline{N}}{\mu + \xi + \alpha}$ generates a bifurcation point between the two equilibria at $R_0 = 1$.

Although we have a variable total population, it is still possible to express the equilibrium-defining system of equations in non-dimensional terms by using the total population at equilibrium $\overline{N}$:

$$\begin{cases} m - R_0 si - ms = 0 \\ R_0 si - i = 0 \\ ai - mr = 0 \end{cases} \tag{6}$$

with the endemic steady state at

$$\begin{cases} s = \dfrac{1}{R_0} \\ i = m\left(1 - \dfrac{1}{R_0}\right) \end{cases}$$

A comparison with the non-fatal disease case shows that differences between the two models lie in the mean duration of infection, respectively $(\mu + \alpha)^{-1}$ and $(\mu + \xi + \alpha)^{-1}$, which is here diminished by the shorter infection life due to disease-related death rate ξ.

2.2 *Models with imbalanced population*

When the population, in absence of the disease, has different birth and death rates ν and μ, then the growth (or decrease) ratio $\dfrac{\mu}{\nu}$ plays a key role in the definition of the

equilibria as a bifurcation point between disease-free and endemic steady states. Moreover, the structural demographic imbalance of the population causes the disease-free population either to grow or to decrease, according to whether $\frac{\mu}{\nu}$ is smaller or larger than 1.

The differences among the imbalanced population models presented in this section lie in the mean duration time of infection, progressively affected by the variable death and birth rate of infectives.

Model 3: Non-fatal Disease Model

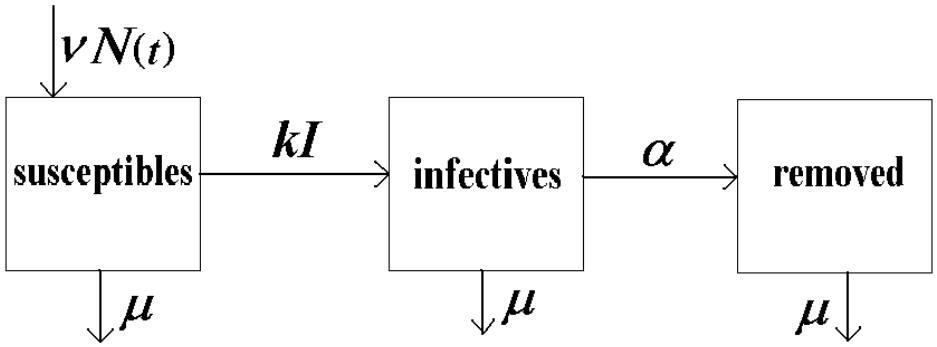

Figure 3: SIR model with variable natural demography

The following system of ODE's describes this model:

$$\begin{cases} \dfrac{dS(t)}{dt} = \nu\big(S(t)+I(t)+R(t)\big) - kS(t)I(t) - \mu S(t) \\ \dfrac{dI(t)}{dt} = kS(t)I(t) - (\mu+\alpha)I(t) \\ \dfrac{dR(t)}{dt} = aI(t) - \mu R(t) \end{cases} \tag{7}$$

When the disease is not present in the population, then the total number of individuals varies exponentially, with a variation sign given by the demographic balance $(\nu - \mu)$: in fact, by substituting $N(t) = S(t) + I(t) + R(t)$ in (7), then $N' = (\nu - \mu)N$. Therefore, if $\nu = \mu$ we have model 1 of the previous section; if, on the other hand, $\nu \neq \mu$ then the sign of $(\nu - \mu)$ determines whether the population becomes extinct (for $\nu < \mu$ we have $N' < 0$) or an endemic equilibrium (for $\nu > \mu$) can be attained at

$$\begin{cases} S = \dfrac{\mu+\alpha}{k} \\ I = \dfrac{\nu N}{\mu+\alpha}\left(1 - \dfrac{\mu}{\nu}\dfrac{1}{R_0}\right) \end{cases} \tag{8}$$

where $R_0 = \dfrac{kN}{\mu+a}$ determines a bifurcation point at $R_0 = \dfrac{\mu}{\nu}$.

The non-dimensional equilibrium is thus given by

$$\begin{cases} s = \dfrac{1}{R_0} \\ i = n\left(1 - \dfrac{m}{n}\dfrac{1}{R_0}\right) \end{cases} \tag{9}$$

Model 4: Fatal Disease Model

Similarly to the models already presented, the analysis of this case is now straightforward: the ODE's system of the model is given by

$$\begin{cases} \dfrac{dS(t)}{dt} = \nu\big(S(t)+I(t)+R(t)\big) - kS(t)I(t) - \mu S(t) \\ \dfrac{dI(t)}{dt} = kS(t)I(t) - (\mu+\xi+\alpha)I(t) \\ \dfrac{dR(t)}{dt} = aI(t) - \mu R(t) \end{cases} \tag{10}$$

with no disease-free equilibrium (unless $\nu = \mu$) and an endemic equilibrium at

$$\begin{cases} S = \dfrac{\mu+\xi+\alpha}{k} \\ I = \dfrac{\nu N}{\mu+\xi+\alpha}\left(1 - \dfrac{\mu}{\nu}\dfrac{1}{R_0}\right) \end{cases} \tag{11}$$

where $R_0 = \dfrac{kN}{\mu+\xi+a}$ determines a bifurcation point at $R_0 = \dfrac{\mu}{\nu}$.

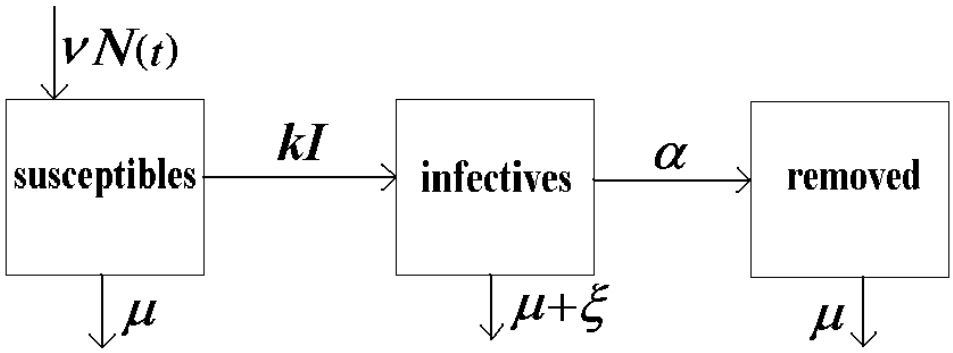

Figure 4: SIR model with variable natural demography and disease-induced deaths

The non-dimensional endemic equilibrium is at

$$\begin{cases} s = \dfrac{1}{R_0} \\ i = n\left(1 - \dfrac{m}{n}\dfrac{1}{R_0}\right) \end{cases} \tag{12}$$

Model 5: Vertical Transmission Model

The vertical transmission (mother-to-child) of an infection is common in two cases: a severe diseases or an environment with degraded hygenic/nutritional conditions. In both cases it seems reasonable to assume a non-negligible disease-induced portion of extra mortality; therefore only a fatal disease model is here illustrated.

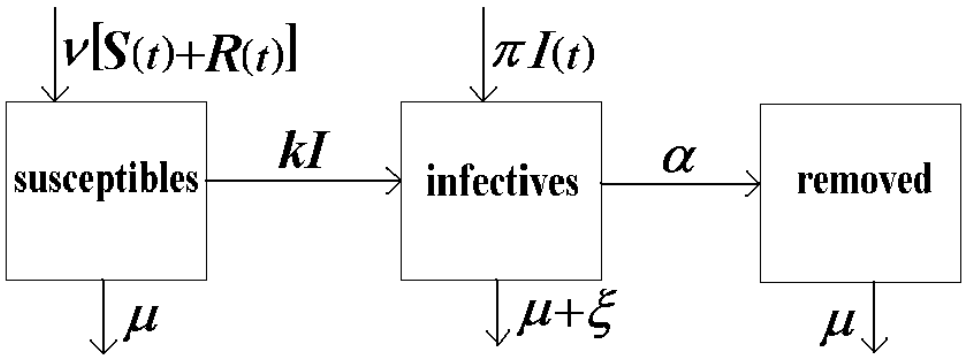

Figure 5: SIR model with variable natural demography, disease-induced-deaths and vertical transmission

The system of ODE's describing the model is given by

$$\begin{cases} \dfrac{dS(t)}{dt} = \nu\big(S(t)+R(t)\big) - kS(t)I(t) - \mu S(t) \\ \dfrac{dI(t)}{dt} = kS(t)I(t) - \big(\mu+\xi+\alpha\big)I(t) + \pi I(t) \\ \dfrac{dR(t)}{dt} = aI(t) - \mu R(t) \end{cases} \tag{13}$$

Similarly to the other imbalanced population models, only an endemic equilibrium is attained if $\nu \neq \mu$:

$$\begin{cases} S = \dfrac{\mu+\xi+\alpha-\pi}{k} \\ I = \dfrac{\nu N}{\mu+\nu+\xi+\alpha-\pi}\left(1 - \dfrac{\mu}{\nu}\dfrac{1}{R_0}\right) \end{cases} \tag{14}$$

with the basic reproduction number now given by $R_0 = \dfrac{kN}{\mu+\xi+a-\pi}$ and a bifurcation point set at $R_0 = \dfrac{\mu}{\nu}$. Given the mean duration of the infectious period $\big(\mu+\xi+\alpha-\pi\big)^{-1}$ the non-dimensional equilibrium is expressed as

$$\begin{cases} s = \dfrac{1}{R_0} \\ i = \dfrac{n}{1+n}\left(1 - \dfrac{m}{n}\dfrac{1}{R_0}\right) \end{cases} \tag{15}$$

2.3 *Models with immigration*

When adding immigration dynamics to the SIR model, then, in general, the resulting ODE's system is no longer autonomous, since the variability of the number of

immigrants $F(t)$ may depend on quantities that are independent of the local population and the study of the equation system presents analytical difficulties that make most of the results impossible to be explicitely expressed.

In this section, two particular cases of autonomous epidemic models will be considered (see Brauer and van der Driessche (2000) and Schinaia (2005)), regarding as variable and constant, alternatively, the immigration flow and the total population, so as not to increase the number of model variables. The two models are, nevertheless, general enough to accommodate a large number of cases, as illustrated in the literature references.

Model 6 : Variable Total Population and Constant Immigration Model

A constant inflow of immigrants into a local population is usually observed when the area of residence of the population is subject to a regular through-flow of individuals: part or all of them (depending on the specific nature of the population, of the area and of the flow) tend to settle in the population and, if the flow and the settling number are constant, then this modelling scheme can be consistently applied. Examples can be found in closed communities such as prisons (see Brauer and van der Driessche (2000)) or

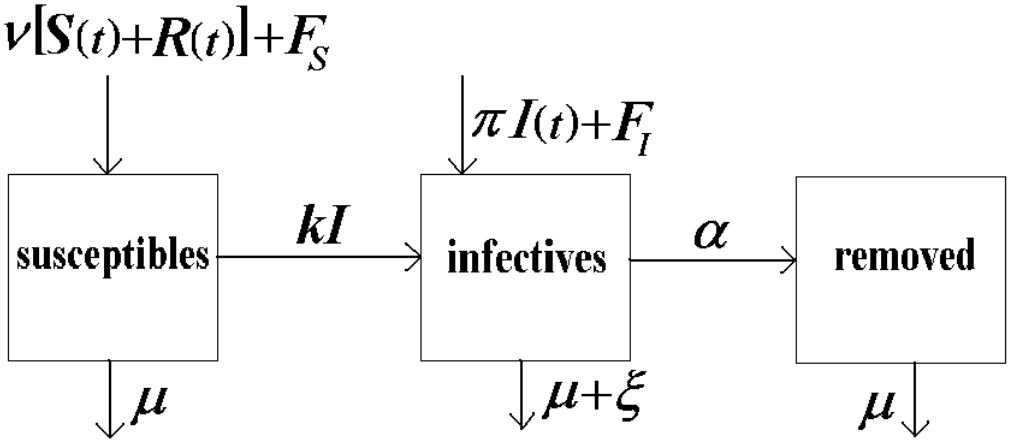

Figure 6: SIR model with variable natural demography, disease-induced-deaths, vertical transmission and constant susceptible/infectious immigration

The equations describing this scheme are given by the following ODE's:

$$\begin{cases} \dfrac{dS(t)}{dt} = \nu\big(N(t) - I(t)\big) - kS(t)I(t) - \mu S(t) + F_S \\ \dfrac{dI(t)}{dt} = kS(t)I(t) - \big(\mu + \xi + \alpha\big)I(t) + \pi I(t) + F_I \\ \dfrac{dN(t)}{dt} = \nu\big(N(t) - I(t)\big) - \mu N(t) + (\pi - \xi)I(t) + F_S + F_I \end{cases} \tag{16}$$

It is both logical and easy to check that no disease-free equilibrium is admitted by this system because of the term F_I in the second equation.

By setting to 0 the derivatives and by dividing the variables by the resulting constant population $\overline{N}$ and the parameters by the mean duration of infection $\big(\mu + \xi + \alpha - \pi\big)^{-1}$ we have the non-dimensional equations

$$\begin{cases} n - ni - R_0 si - ms + f_S = 0 \\ R_0 si - i + f_I = 0 \end{cases} \tag{17}$$

where $R_0 = \dfrac{kN}{\mu + \xi + a - \pi}$ and whose solutions are given by

$$\begin{cases} s = \dfrac{i - f_I}{R_0 i} \\ i = \dfrac{1}{2(n+1)}\left(n + f_I + f_S - \dfrac{m}{R_0}\right) \pm \sqrt{\left[\dfrac{1}{2(n+1)}\left(n + f_I + f_S - \dfrac{m}{R_0}\right)\right]^2 + \dfrac{1}{2(n+1)}\dfrac{2mf_I}{R_0}} \end{cases} \tag{18}$$

It is easy to check that *i* is positive only for the positive sign before the square root and for $n + f_I + f_S > \dfrac{m}{R_0}$. Therefore we must have $R_0 > \dfrac{m}{n + f_I + f_S}$ or, in terms of the original parameters, $R_0 > \dfrac{\mu}{\nu + F_I + F_S}$.

Model 7: Constant Total Population and Variable Immigration Model

A geographical area with limited resources can only host a maximum of, say *N* individuals and, if there is sufficient demographic pressure on its borders, then the saturation level *N* tends to be attained either by local newborns or, when a negative imbalance is observed in the local community, by immigration or emigration when the imbalance is positive (see Schinaia, 2005). In these cases the total population under study is constant and the inflow/outflow of individuals is variable and depends on the natural and disease-induced demographic dynamics.

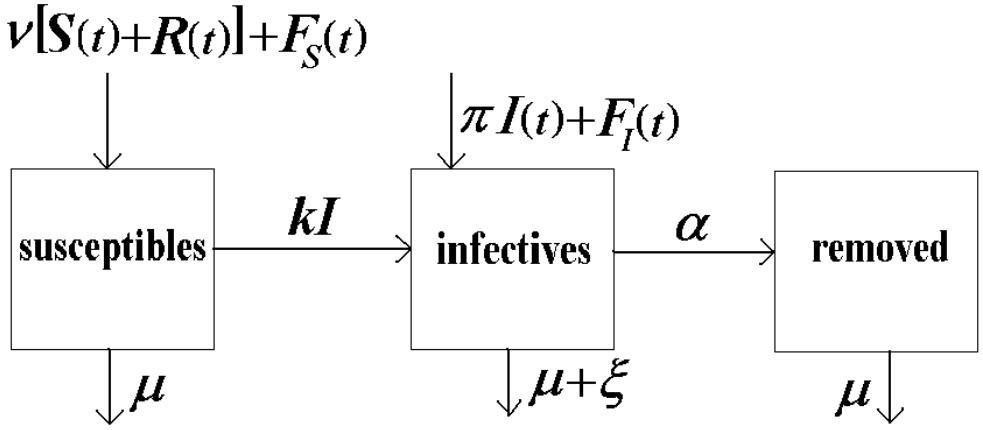

Figure 7: SIR model with variable natural demography, disease-induced-deaths, vertical transmission and variable susceptible/infectious immigration

If vertical transmission is also assumed, then the following ODE's describe the system:

$$\begin{cases} \dfrac{dS(t)}{dt} = \nu\big(S(t)+R(t)\big) - kS(t)I(t) - \mu S(t) + F_S(t) \\ \dfrac{dI(t)}{dt} = kS(t)I(t) - \big(\mu+\xi+\alpha\big)I(t) + \pi I(t) + F_I(t) \\ \dfrac{dR(t)}{dt} = aI(t) - \mu R(t) \end{cases} \tag{19}$$

where the total population is variable, according to $\dfrac{dN(t)}{dt} = \dfrac{dS(t)}{dt} + \dfrac{dI(t)}{dt} + \dfrac{dR(t)}{dt}$ and where the total inflow $F(t) = F_S(t) + F_I(t)$, split into $(1-p)\%$ of susceptibles and $p\%$ of infectives is given by the global imbalance of the population; i.e.,

$$\begin{cases} F_S(t) = (1-p)\big[(\mu-\nu)\big(S(t)+R(t)\big) + \big(\mu-\pi+\xi\big)I(t)\big] \\ F_I(t) = p\big[(\mu-\nu)\big(S(t)+R(t)\big) + \big(\mu-\pi+\xi\big)I(t)\big] \end{cases} \tag{20}$$

The ODE's of the system can be thus written as

$$\begin{cases} \dfrac{dS(t)}{dt} = \nu\big(S(t)+R(t)\big) - kS(t)I(t) - \mu S(t) + (1-p)\big[(\mu-\nu)\big(S(t)+R(t)\big) + \big(\mu-\pi+\xi\big)I(t)\big] \\ \dfrac{dI(t)}{dt} = kS(t)I(t) - \big(\mu+\xi+\alpha\big)I(t) + \pi I(t) + p\big[(\mu-\nu)\big(S(t)+R(t)\big) + \big(\mu-\pi+\xi\big)I(t)\big] \\ \dfrac{dR(t)}{dt} = aI(t) - \mu R(t) \end{cases} \tag{21}$$

By setting to 0 $\dfrac{dN(t)}{dt} = \dfrac{dS(t)}{dt} + \dfrac{dI(t)}{dt} + \dfrac{dR(t)}{dt} = 0$ and by dividing the variables by the resulting constant population $\overline{N}$ and the parameters by the mean duration of infection $\big(\mu + (1-p)\big(\xi-\pi\big) - p\nu + P(\mu-\nu)\big)^{-1}$ we have the non-dimensional equations

$$\begin{cases} -R_0 si + (m-a) - ms + bi = 0 \\ R_0 si - i + a = 0 \end{cases} \tag{22}$$

where $R_0 = \dfrac{kN}{\mu + (1-p)\big(\xi-\pi\big) - p\nu + \alpha}$ and $a = p(\mu-\nu)$ and whose solutions are given by

$$\begin{cases} s = \dfrac{i-a}{R_0 i} \\ i = \dfrac{m}{2(1-b)}\left(1-\dfrac{1}{R_0}\right) \pm \sqrt{\left(\dfrac{m}{2(b-1)}\right)^2\left(1-\dfrac{1}{R_0}\right)^2 + \dfrac{2am}{2(b-1)}} \end{cases} \tag{23}$$

Similarly to model 6., it is easy to check that *i* is positive only for the positive sign before the square root; however, the positivity of *i* involves simultaneous conditions on R_0 and *a*. A thoughrough analysis of this model can be found in Schinaia, 2005.

Table 1: summary of asymptotic features of the various SIR models. The first column refers to the figure numbering and in the threshold column there are the parameter values where the phase transition between disease-free and endemic equilibrium occurs

model	R_0	bifurcation threshold	equilibria
1.	$\frac{kN}{\mu + a}$	$R_0 = 1$	**d-f / end**
2.	$\frac{kN}{\mu + \xi + \alpha}$	$R_0 = 1$	**d-f**
3.	$\frac{kN}{\mu + \alpha}$	$R_0 = \frac{\mu}{\nu}$	**yes**
4.	$\frac{kN}{\mu + \xi + \alpha}$	$R_0 = \frac{\mu}{\nu}$	**yes**
5.	$\frac{kN}{\mu + \xi + a - \pi}$	$R_0 = \frac{\mu}{\nu}$	**yes**
6.	$\frac{kN}{\mu + \xi + a - \pi}$	$R_0 = \frac{\mu}{\nu + F_I + F_S}$	**no**
7.	$\frac{kN}{\mu + (1-p)(\xi - \pi) - p\nu + \alpha}$	$R_0 = 1$ $a = p(\mu - \nu) = 0$	**no**

3. Testing Modelling Hypothesis

When designing a model to describe the diffusion of an epidemic in a population, the several aspects involved in the modelling process are shaped according to hypotheses considered plausible from biological, clinical and demographic viewpoints. Such

plausibility stems from *in vitro* biology experiments and socio-demographic observations: while, on the one hand, the former can be controlled by the researcher along with its statistical significance, the latter, on the other hand, can only be used in the model *'as is'* , without much possibility of significance analysis because of their structural irrepetibility. In this light, it becomes essential an *'a posteriori'* analysis of the consistency of the whole mathematical structure: when overall data on the epidemic diffusion are available (such as those from public health surveillance systems), then such analysis is necessarily in the classical form of parametric or non-parametric hypothesis testing of theoretical results on the basis of observed data.

3.1 *Non-parametric Testing: Model Comparisons*

The most common epidemiological data on infectious diseases are those usually provided by surveillance systems; in general, they include longitudinal data sets of incidence cases in a reference population, sometimes in the form of non-dimensional incidence rates. In some more closely surveilled epidemics, also prevalence cases are available, possibly along with further information on the observed disease progression. Often, reporting delay, underreporting or other forms of environmental blur affect the official data and adjustement techniques have to be expressely developped and applied to polish the numerical information and make them usable in modelling and forecasting studies (bibliografia).

A simple, euristic way of testing the various modelling hypothesis is based on a non parametric comparison of empirical an time series curve, derived from the available

data, and the corresponding simulated time series curve, obtained from the theoretical model. Let us suppose that O_i be the observed incidence cases at times t_i $i = 1;...;n$ and that $E(t_i)$ be the corresponding simulated incidence, using the model to be tested.

3.2 *Parametric Testing*

The models presented in the previous section follow a hyerarchical order in the sense that, by progressively eliminating specific parameters, it is possible to regard the various models as 2-dimensional nested into each other. In this fashion, for instance, R_0 of model 6. is a particular case of R_0 of model 7. with $p = 0$ but the reverse is valid for the threshold (R_0 threshold of 7. is a particular case of the same of 6. under appropriate hypotesis). Therefore, ascending the hyerarchy, models 2. and 5. can be considered as "null hypothesis" models for, respectively, disease-free population imbalance and infectious immigration alternative hypothesis for a fatal disease: similarly, each lower order model can be considered as a "null" model for some alternative hypothesis on the higher order one. By using appropriate data, a statistical hypothesis testing procedure can be carried out on the basis of some parameter properties of epidemic models.

Let us consider the steady state proportion of susceptibles $\bar{s} = \frac{\bar{S}}{N}$ in a population of N individuals: data on $\bar{S}$ can be obtained by random sample blood testing results on K individuals, as suggested in Diekmann and Heesterbeek (2000). Note, however, that this is only possible when immunity does not erase all traces of the former infection (i.e., B

hepatitis, tuberculosis, etc.): in fact, in such a case the r.v.'s $\hat{\sigma}_j$ and $\hat{\rho}_j$, $j = 1,\ldots,K$, are the indicators of each of the admissible patient status:

$$\hat{\sigma}_j = \begin{cases} 0 & \text{negative testing} \\ 1 & \text{positive testing} \end{cases} \qquad \hat{\rho}_j = \begin{cases} 0 & \text{inactive infection} \\ 1 & \text{active infection} \end{cases}$$

thus making the estimate $\hat{S}$ of $\overline{S}$ a binomial random variable, sum of the blood testing results $\hat{S} = K - \sum_j \hat{\sigma}_j$ and $\hat{s} = \frac{\hat{S}}{K}$ the ML estimate of the proportion $\overline{s}$. By the invariance property of the ML estimators, we have $\hat{R}_0 = \frac{1}{\hat{s}}$ and, using the appropriate threshold bifurcation value of R_0, we can predict whether the infection is persistant in the population (i.e., whether we are observing a transient outburst or the infection is permanently settling) with the following systems of hypothesis

$$\begin{cases} H_0 : R_0 < r \\ H_1 : R_0 > r \end{cases}$$

where *r* is a value chosen according to the third column in table 1 of the type of model considered.

Furthermore, using the same data set as above, it is possible estimate $\hat{i}$ of the proportion of infectives in the population by $\hat{i} = \frac{1}{K}\sum_j \hat{\sigma}_j \times \hat{\rho}_j$. Now, recalling (18), we have that $\hat{f}_I = \hat{i} - \hat{R}_0 \hat{s}\hat{i}$ is the ML estimate of the proportion of infectious

immigration in model 6. (time constant immigration) and it can be used as a test statistic for an appropriate nullity test:

$$\begin{cases} H_0 : f_I = 0 \\ H_1 : f_I > 0 \end{cases}$$

By recalling that $a = p(\mu - \nu)$ from (23), the equivalent estimate in model 7. (time constant population), given by $\hat{a} = \hat{i} - \hat{R}_0 \hat{s} \hat{i}$, can be similarly used for testing

$$\begin{cases} H_0 : p = 0 \\ H_1 : p > 0 \end{cases}$$

The estimate $\hat{a}$ presents, however, the inconvenient of being admissible only with imbalanced disease-free population: in fact, in terms of original parameters, we have $a = p(\mu - \nu)$ and, if $\mu = \nu$, then $a = 0$ independently of the value of *p*, thus introducing an inconsistency factor in the process. In fact, in such a case, as from (23), the endemic equilibrium proportion of infectives is given by $i = \frac{m}{1-b}\left(1 - \frac{1}{R_0}\right)$, or, in terms of original parameters, $i = \frac{\mu}{\mu + \alpha}\left(1 - \frac{1}{R_0}\right)$. However, if further information is available on the clinical/biological progression of the infection and values can be assigned to the model parameters *k*, β, μ, π, ξ and α then the expression $S = \frac{(1-p)(\mu + \pi - \xi) + \alpha}{k}$ can be solved for *p* and expressed in terms of estimate $\hat{S}$ as $\hat{p} = 1 + \frac{\alpha - k\beta\hat{S}}{\mu + \pi - \xi}$ and used as a test statistic to test the nullity of infectious immigration in a population at disease-free equilibrium.

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