SUMMER SCHOOL

on

Mathematical Models in Life Science:
Theory and Simulation

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THE MATHEMATICAL MODELING OF EPIDEMICS

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Lecture 2: The disease clock

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Nunc ratio quae sit morbis aut unde repente
mortiferam possit cladem conflare coorta
morbida vis hominum generi peducumque catervis,
expediam. Primum multarum semina rerum
esse supra docui quae sint vitalia nobis,
et contra quae sint morbo mortique necessest
multa volare. Ea cum casu sunt forte coorta
et perturbarunt caelum, fit morbidus aer.[1]

Lucretius
"De Rerum Natura", Liber VI, 1090-1097

The S-I-R model that we have presented in the previous lecture is usually named after Kermack and McKendrick ([5]-[7], [8]) who, in a celebrated paper provided the basic framework for subsequent research in the field of modeling epidemics. This very first and celebrated epidemic model was actually structured by *class-age*, i.e. the time elapsed since an individual became infected: this is important when modeling a long time lasting disease for which an infected individual has a variable chance of recovery or death and his infectiveness also depends on the time spent as an infected. The recent epidemics by HIV/AIDS infection well represents this latter phenomenology and also the specific features of a disease such as Tuberculosis motivate the use of *class-age* in the models. As a matter of fact, for a long time the simplified S-I-R model has been the main tool for analyzing epidemics and still models based on ODE's are currently used providing significant results. However, in recent years the original Kermack-McKendrick model has attracted new interest especially in connection with emerging diseases such as AIDS and TB.

[1] Now what is the cause of plagues, and whence on a sudden the force of disease can arise and gather deadly destruction for the race of men and the herds of cattle, I will unfold. First I have shown before that there are seeds of many things which are helpfull to our life, and on the other hand it must needs be that many fly about which cause disease and death. And when by chance they have appened to gather and distemper the sky, then the air becomes full of disease.

1 The Kermack-McKendrick model

As a first step we consider a closed population in which no migration is present and no births or deaths occur from natural reasons. This assumption, of course, is realistic as long as we want to describe the single outbreak of an epidemic through a period of time such that demographic changes can be disregarded. In this case, the "clock of the disease" is faster than the demographic processes. Thus, the total number of individuals, that we denote by N, is constant as in the model of Lecture 1 and the population is as usual partitioned into the three subclasses of susceptibles, infectives and removed individuals, but the class if infectives is now structured. In fact, for a member of the infected class we will

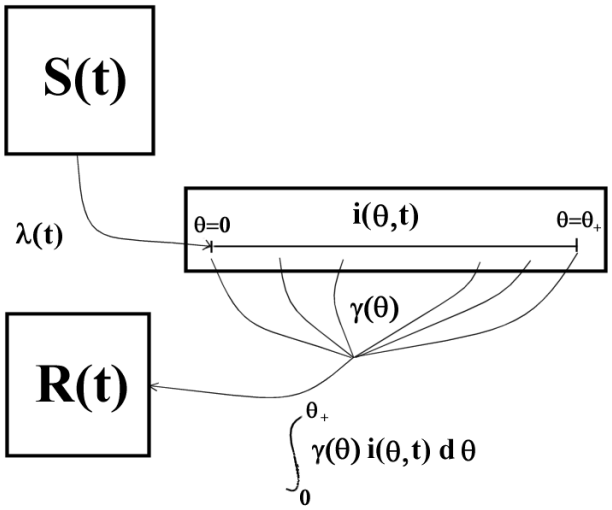

Figure 1: A sketch of the Kermack-McKendrick model

denote by $\theta \in [0, \theta_\dagger]$ the time elapsed since infection ($\theta_\dagger$ denotes a maximum age of infection); then the state of the process is described by the following variables

$$\begin{array}{ll} S(t) & = \textit{number of susceptible individuals at time } t, \\ i(\theta,t) & = \theta\textit{-density of infected individuals at time } \ t, \\ R(t) & = \textit{number of removed individuals at time } \ t. \end{array}$$

Of course we must have

$$S(t) + \int_0^{\theta_\dagger} i(\theta,t)d\theta + R(t) = N.$$

In addition we consider the following parameters:

$$\begin{array}{l} \gamma(\theta) = \textit{age-specific removal rate,} \\ \lambda(t) = \textit{infection rate (force of infection).} \end{array}$$

Thus,

$$\gamma(\theta)i(\theta,t)d\theta dt$$

denotes the number of infected individuals, with class age in the interval $[\theta, \theta + d\theta]$, that pass into the removed class during the time interval $[t, t+dt]$; moreover,

$$\lambda(t)S(t)$$

is again the *incidence*, i.e. the number of susceptible individuals becoming infected in a time unit.

Actually the force of infection $\lambda(t)$ must be given a constitutive form describing the mechanism of infection. The simplest form, extending the constitutive form of the non-structured case, is the following:

$$\lambda(t) = \int_0^{\theta_\dagger} \lambda_0(\theta) i(\theta, t) d\theta, \tag{1}$$

where

$$\lambda_0(\theta) = \frac{c(\theta)\chi(\theta)}{N}, \tag{2}$$

with both the contact rate and the infectiveness possibly depending on the disease progression.

Following the sketch of Figure 1, the equations of the model turn out to be:

$$\begin{cases} i) & S'(t) = -\lambda(t)S(t) \\ ii) & i_t(\theta, t) + i_\theta(\theta, t) + \gamma(\theta) i(\theta, t) = 0 \\ iii) & i(0, t) = \lambda(t)S(t) \\ iv) & R'(t) = \int_0^{\theta_\dagger} \gamma(\theta) i(\theta, t) d\theta, \end{cases} \tag{3}$$

with the initial conditions:

$$S(0) = S_0, \quad i(\theta, 0) = i_0(\theta), \quad R(0) = R_0.$$

In (3) equation $ii)$ is related to the disease progression and condition $iii)$ is a non-local boundary condition modelling the input of new infectives at age $\theta = 0$. We note that, with the constitutive form (1) the equations $i)$, $ii)$, $iii)$ of system (3) are decoupled from $iv)$ so that, for the study of the system, it is enough to consider the first three equations. We will treat the problem under the following assumptions on the parameters:

$$\gamma(\theta) \geq 0, \quad \lambda_0(\theta) \geq 0 \quad a.e.\ in\ \ [0, \theta_\dagger], \tag{4}$$

$$\gamma(\cdot) \in L^1_{loc}(0, \theta_\dagger), \quad \int_0^{\theta_\dagger} \gamma(\sigma) d\sigma = +\infty, \tag{5}$$

$$\lambda_0(\cdot) \in L^\infty(0, \theta_\dagger), \quad \lambda_0(\theta) > 0 \quad a.e.\ in\ \ [\theta_1, \theta_2]. \tag{6}$$

2 Reduction of the system

The non-local condition (3, iii) takes into account the age of the infectives over all the age interval $[0, \theta]$, thus introducing a dependence of the solution from the past history of the system. In fact we can reduce (3) into a system of integro-differential equations, starting from the integrated formula

$$i(\theta, t) = \begin{cases} i_0(\theta - t)\dfrac{B(\theta)}{B(\theta - t)} & if \quad \theta \geq t \\ i(0, t - \theta)B(\theta) & if \quad \theta < t, \end{cases} \tag{7}$$

where we have set

$$B(\theta) = e^{-\int_0^\theta \gamma(\sigma)d\sigma}.$$

Formula (7) follows by integration of $(3, ii)$ along the characteristic lines $\theta - t = const$, using the initial datum $i_0(\theta)$ and $i(0,t)$ as boundary boundary values (see Figure 2).

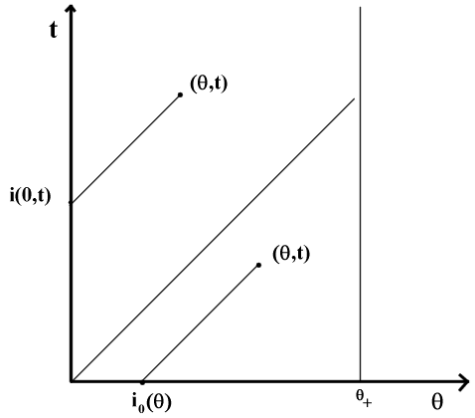

Figure 2: Integration along the characteristic lines

Then, we consider the incidence as a convenient scalar variable:

$$\sigma(t) = \lambda(t)S(t) = \ i(0,t),$$

from which we can get $i(\theta,t)$, using formula (7). We have (see (1))

$$\begin{aligned}\sigma(t) \ &= \int_0^{\theta_\dagger} \lambda_0(\theta) i(\theta,t) d\theta \ S(t) = \\ &= \left[\int_0^t \lambda_0(\theta)B(\theta)\sigma(t-\theta)d\theta \ + \ \int_t^\infty \lambda_0(\theta)\frac{B(\theta)}{B(\theta-t)} i_0(\theta-t)d\theta\right] S(t),\end{aligned}$$

where $\lambda_0(\theta)$, $B(\theta)$, $i_0(\theta)$ are extended by zero outside of $[0, \theta_\dagger]$. Thus, we have the following system in the variables $\sigma(t)$ and $S(t)$:

$$\left\{\begin{array}{l} S'(t) = -\sigma(t) \\ \sigma(t) = \left[\int_0^t A(t-s)\sigma(s)ds \ + \ F(t)\right] S(t), \end{array}\right. \tag{8}$$

where

$$\left\{\begin{array}{l} A(t) = \ \lambda_0(t) \ B(t) \\ F(t) = \ \int_0^\infty \lambda_0(t+s)\frac{B(t+s)}{B(s)} i_0(s)ds, \end{array}\right. \tag{9}$$

with the initial condition:

$$S(0) = S_0 > 0. \tag{10}$$

Concerning existence and uniqueness of a global solution to (8) we have (see for instance [4])

Theorem 1 *Let (4)-(6) be verified and let* $i_0 \in L^1[0,\theta_\dagger]$. *Then problem (8) with (9) and (10) has a unique solution* $(\sigma(t), S(t))$ *with:*

$$\sigma(t) \geq 0, \quad \sigma(\cdot) \text{ continuous on } [0,+\infty),$$

$$S(t) \geq 0 \quad , \quad S(\cdot),\ S'(\cdot) \text{ continuous on } [0,+\infty).$$

Proof.

To prove the thesis of the theorem it is convenient to transform (8) into a single equation. In fact, since

$$S'(t) = -\left[\int_0^t A(t-s)\sigma(s)ds + F(t)\right] S(t),$$

we have

$$S(t) = S_0 e^{-\left[\int_0^t A_1(t-s)\sigma(s)d\sigma + F_1(t)\right]}, \tag{11}$$

where $A_1(t) = \displaystyle\int_0^t A(s)ds$, $F_1(t) = \displaystyle\int_0^t F(s)ds$; then (8) is equivalent to

$$\sigma(t) = S_0 \left[\int_0^t A(t-s)\sigma(s)ds \ + \ F(t)\right] e^{-\left[\int_0^t A_1(t-s)\sigma(s)ds + F_1(t)\right]}. \tag{12}$$

Now $F(t)$, $F_1(t)$ are non-negative, continuous, and bounded on $[0,+\infty)$, while $A(t)$, $A_1(t)$ are non-negative a.e. and belong to $L^\infty(0,+\infty)$; thus the mapping $\mathcal{T} : C[0,T] \to C[0,T]$ defined as

$$(\mathcal{T}v)(t) = S_0 \left[\int_0^t A(t-\sigma)v(\sigma)d\sigma \ + \ F(t)\right] e^{-\left[\int_0^t A_1(t-\sigma)v(\sigma)d\sigma + F_1(t)\right]}$$

leaves the set

$$v(\cdot) \in C[0,T]; \quad 0 \leq v(t) \leq S_0 |F|_\infty e^{S_0 |A|_\infty t}$$

unchanged and, moreover, for v and $\bar{v}$ belonging to this set,

$$\left|\mathcal{T}^N v - \mathcal{T}^N \bar{v}\right|_{C[0,T]} \leq \frac{C^N T^N}{N!} |v - \bar{v}|_{C[0,T]}$$

where C is a constant. Thus, existence and uniqueness of a continuous solution to (12) follows as a fixed point of $\mathcal{T}$.

Finally, by (11), we get $S(t)$.

∎

In the following section we will use (8) for analyzing the asymptotic behavior of (3).

3 Epidemic outbreak and extinction

The Kermack-McKendrick model, though more structured than the SIR model based on ODE's, provides a similar description of the epidemic ([4]). In fact we first have:

Theorem 2 *Let $(\sigma(t), S(t))$ be the solution to (8) provided by Theorem 1. Then we have*

$$\lim_{t\to+\infty} \sigma(t) = 0, \quad \lim_{t\to+\infty} S(t) = S_\infty, \tag{13}$$

where S_∞ satisfies

$$S_\infty = S_0 \exp\left[S_\infty \int_0^\infty A(s)ds + \int_0^\infty F(s)ds - S_0\right]. \tag{14}$$

Proof:

We first note that, from (8),

$$S(t) = S_0 \; - \; \int_0^t \sigma(s)ds > 0,$$

so that

$$\int_0^\infty \sigma(s)ds \leq \; S_0 \tag{15}$$

and

$$\lim_{t\to+\infty} S(t) = \; S_\infty \; = \; S_0 \; - \; \int_0^\infty \sigma(s)ds \geq 0.$$

Also,

$$F(t) = 0 \quad for \quad t > \theta_\dagger,$$
$$A(t) = 0 \quad for \quad t > \theta_\dagger,$$

so that, since by (13) $\sigma \in L^1(0, +\infty)$, we have

$$\lim_{t\to+\infty} \int_0^t A(t-s)v(s)ds = 0.$$

In conclusion, passing to the limit in (12), (13) is proved.

Concerning the final size of the susceptible class, since $\sigma(t) = -S'(t)$, from (11) we get

$$\begin{aligned} S(t) \quad &= S_0 \exp\left[\int_0^t A_1(t-s)S'(s)ds \; + \; F_1(t)\right] = \\ &= S_0 \; \exp\left[\int_0^t A(s)S(t-s)ds \; + \; F_1(t) - S_0\right] \end{aligned}$$

so that, passing to the limit, we have (14).

∎

The previous theorem states two main facts about the single epidemic: the infection eventually dies out but the susceptible class is not depleted by the epidemic. In fact,

$$\lim_{t\to+\infty} I(t) = \lim_{t\to+\infty} \int_0^{\theta_\dagger} i(\theta, t)d\theta = \lim_{t\to+\infty} \int_0^\infty \sigma(t-\theta)B(\theta)d\theta = 0$$

and also, by (14), it must be $S_\infty > 0$.

Another important aspect of the dynamics of an epidemic is the existence of a threshold in order that the infection be sustained. To introduce this threshold we must first prove:

Proposition 1 *Under the conditions of Theorem 1, $\sigma(t)$ is either identically zero or eventually positive. If, in addition*

$$\lambda_0(\theta) > 0 \quad a.e.\ in \quad [0, \theta_\dagger], \tag{16}$$

then $\sigma(t)$ is positive for all $t \geq 0$.

Proof.

We prove the thesis by contradiction. In fact, if $\sigma(t)$ is not identically zero, let

$$\sigma(t) > 0 \quad for \quad t \in [\alpha, \beta].$$

Then, using (6), for $t \in\ [\alpha + \theta_1\ ,\ \beta + \theta_2]$ we have

$$\begin{aligned}
\sigma(t) \quad &\geq S(t) \int_0^t A(t-\theta)\sigma(\theta)d\theta \ \geq\ S(t) \int_\alpha^{t\wedge\beta} A(t-\theta)\sigma(\theta)d\theta \geq \\
&\geq S(\beta+\theta_2) \min_{\theta\in[\alpha,\beta]} \sigma(\theta) \int_\alpha^{t\wedge\beta} A(t-\theta)d\theta \ = \\
&= S(\beta+\theta_2) \min_{\theta\in[\alpha,\beta]} \sigma(\theta) \int_{0\vee(t-\beta)}^{t-\alpha} \lambda_0(\theta)B(\theta)d\theta \ > 0.
\end{aligned}$$

In fact, $(\theta_1, \theta_2) \cap (0 \vee (t-\beta)\ ,\ t-\alpha) \neq \emptyset$ and $S(\beta + \theta_2) > 0$.

Iterating this argument we prove that:

$$\sigma(t) > 0 \quad for \quad t\ \in\ [\alpha + n\theta_1\ ,\ \beta + n\theta_2],$$

for any positive integer n and, consequently, $\sigma(t)$ is eventually positive.

Let now (14) be satisfied, then $F(0) > 0$ and, consequently, $\sigma(0) > 0$. If $\sigma(t)$ vanishes somewhere, there must exist t_0 such that

$$\sigma(t_0) = 0, \quad \sigma(t) > 0 \quad for \quad t \in [0, t_0).$$

Then we must have:

$$\begin{aligned}
0 = \sigma(t_0) \quad &= S(t_0) \left[\int_0^{t_0} A(t_0 - s)\sigma(s)ds \ +\ F(t_0) \right] \geq \\
&\geq S(t_0) \int_0^{t_0} A(t_0 - s)\sigma(s)ds \ > 0,
\end{aligned}$$

which is impossible; so it must be $\sigma(t) > 0$ for all $t \geq 0$.

∎

If we now set $I_k = [k\theta_\dagger, (k+1)\theta_\dagger] \quad (k = 1, 2 \dots)$ and define

$$m_k = \min_{t\in I_k} \sigma(t), \quad M_k = \max_{t\in I_k} \sigma(t), \quad S_k = S(k\theta_\dagger)$$

we have the following immediate consequence of the previous proposition:

Proposition 2 *Let*

$$M_k > 0 \quad for\ all \ \ k \geq 0 \quad and \quad m_k > 0 \quad eventually.$$

If (14) is satisfied, then $m_k > 0$ for all $k \geq 0$.

Proof:

First we note that, since $F(t)$ is not identically zero on $[0, \theta_\dagger]$, neither is $\sigma(t)$ and we have $M_0 > 0$. Besides, assume $M_k > 0$ and let $[\alpha, \beta] \subset I_k$ be such that $\sigma(t) > 0$ on $[\alpha, \beta]$; then, by the proof of Proposition 1, $\sigma(t) > 0$ on $[\alpha + n\theta_1, \beta + n\theta_2]$. Since it is possible to find n such that $(k+1)\theta_\dagger < \alpha + n\theta_1 < (k+2)\theta_\dagger$, it is also $\sigma(t) > 0$ somewhere in I_{k+1} and, consequently, also $M_{k+1} > 0$.

The last part of the thesis is a straightforward consequence of Proposition 1.

∎

Also in the present case we may define a basic reproduction number as

$$\mathcal{R}_0 = \int_0^{\theta_\dagger} c(\theta)\chi(\theta)B(\theta)d\theta = N\int_0^{\theta_\dagger} A(\theta)d\theta. \tag{17}$$

This again represents the number of secondary case produced by one infective, during the whole time of the disease. Now, the variability of the parameters with respect to the age θ is taken into account. The condition for an epidemic outbreak is stated in the following theorem.

Theorem 3 *Let (14) be satisfied. Then, for $k > 0$:*

$$\textit{if} \quad \mathcal{R}_0\frac{S_k}{N} < 1 \quad \textit{then} \quad M_k < M_{k-1} \tag{18}$$

$$\textit{if} \quad \mathcal{R}_0\frac{S_{k+1}}{N} > 1, \quad \textit{then} \quad m_k > m_{k-1}; \tag{19}$$

moreover, we have

$$\mathcal{R}_0\frac{S_\infty}{N} < 1. \tag{20}$$

Proof:

To prove (18) let $t \in I_k$ with $k > 0$; then

$$\sigma(t) = S(t)\int_0^{\theta_\dagger} A(s)\sigma(t-s)ds.$$

Since $(t-s) \in I_k \cup I_{k-1}$ for $s \in [0, \theta_\dagger]$, we have

$$\sigma(t) \leq S(t) \int_0^{\theta_\dagger} A(s)ds \ \max[M_k, M_{k-1}],$$

$$M_k \leq \mathcal{R}_0\frac{S_k}{N} \ \max[M_k, M_{k-1}],$$

so that, since $M_k > 0$, we have

$$M_k < \max[M_k, M_{k-1}],$$

and (18) is proved. The proof of (19) is analogous. Concerning (20), assume by contradiction that $\mathcal{R}_0\frac{S_k}{N} > 1$ for all k; then, by (19), the sequence m_k is increasing, which is impossible by (13).

∎

The previous theorem allows to give a detailed description of how the epidemics evolves through the sequence of time steps whose length is $\theta_\dagger$. For instance we see that, if at the end of the first step the number of susceptibles is under the threshold $\dfrac{N}{\mathcal{R}_0}$, then the epidemics will not be sustained.

4 The S-I-S model: endemic states and stability

In the previous section we have seen that the threshold mechanism leading to the epidemic outbreak is confirmed within the context of age structured modeling. Actually the structured version of the Kermack-McKendrick model provides a threshold parameter tuned by the effect of parameters variability as a function of age. Here we consider the structured version of the S-I-S model in order and set up the methods to investigate endemic states and their stability.

The S-I-S model is sketched in Figure 3 and the equations of the model are an obvious modification of system (3).

$$\begin{cases} i) & S'(t) = -\lambda(t)S(t) + \displaystyle\int_0^{\theta_\dagger} \gamma(\theta) i(\theta,t) d\theta \\ ii) & i_t(\theta,t) + i_\theta(\theta,t) + \gamma(\theta) i(\theta,t) = 0 \\ iii) & i(0,t) = \lambda(t) S(t) \end{cases} \tag{21}$$

with the initial conditions:

$$S(0) = S_0, \quad i(\theta,0) = i_0(\theta).$$

and with the constitutive equation (1).

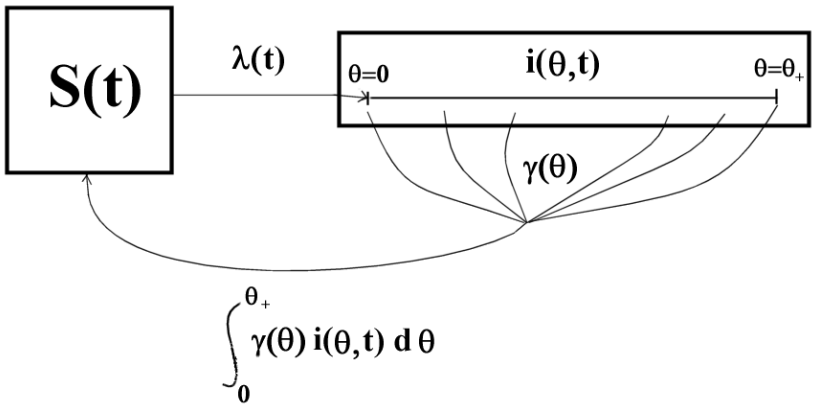

Figure 3: The S-I-S model with age structure

We note that considering the total number of infectives

$$I(t) = \int_0^{\theta_\dagger} i(\theta,t) d\theta,$$

and integrating (21, ii) with respect to θ we have:

$$\begin{aligned} I'(t) &= i(0,t) - i(\theta_\dagger, t) - \int_0^{\theta_\dagger} \gamma(\theta) i(\theta, t) d\theta \\ &= \lambda(t) S(t) - \int_0^{\theta_\dagger} \gamma(\theta) i(\theta, t) d\theta. \end{aligned}$$

This implies

$$\frac{d}{dt}\left(S(t) + I(t)\right) = 0$$

and, consequently, the following equation

$$S(t) + I(t) = N, \tag{22}$$

where N must be the same constant that appears in (2) to guarantee model consistency. Equation (22) allows to reduce the problem to a single integral equation of Volterra convolution type. In fact, taking the incidence $\sigma(t)$ as a key variable, we have

$$\begin{aligned} \lambda(t) &= \int_0^t A(s)\sigma(t-s)ds + \Lambda_0(t) \\ S(t) &= N - I(t) = N - \int_0^t B(s)\sigma(t-s)ds - I_0(t) \end{aligned}$$

and

$$\sigma(t) = \left(N - \int_0^t B(s)\sigma(t-s)ds + I_0(t)\right)\left(\int_0^t A(s)\sigma(t-s)ds + \Lambda_0(t)\right). \tag{23}$$

where

$$\Lambda_0(t) \to 0, \quad I_0(t) \to 0,$$

as $t \to \infty$.

The search for steady (endemic) states of system (21) is then equivalent to the search for constant solution of the "limiting equation" of (23)

$$\sigma(t) = \left(N - \int_0^\infty B(s)\sigma(t-s)ds\right)\int_0^\infty A(s)\sigma(t-s)ds. \tag{24}$$

In fact, a steady solution $(S_*), i_*(\theta))$ of (21) must satisfy

$$\begin{cases} i) & 0 = -\lambda_* S_* + \int_0^{\theta_\dagger} \gamma(\theta) i_*(\theta) d\theta, \\ ii) & i_*'(\theta + \gamma(\theta) i_*(\theta) = 0, \\ iii) & i(0) = \lambda_* S_*, \\ iv) & \lambda_* = \displaystyle\int_0^{\theta_\dagger} \lambda_0(\theta) i_*(\theta) d\theta, \\ v) & S_* + \displaystyle\int_0^{\theta_\dagger} i_*(\theta) d\theta = N. \end{cases} \tag{25}$$

Then, after the *disease free* solution

$$S_* = N, \quad i_*(\theta) = 0, \tag{26}$$

by *ii*) and *iii*) we get

$$i_*(\theta) = \lambda_* S_* B(\theta),$$

that, substituted in *iv*) and *v*), yields

$$S_* = \frac{N}{\mathcal{R}_0} \quad \text{and} \quad i_*(\theta) = \frac{N}{\mathcal{B}} \left(1 - \frac{1}{\mathcal{R}_0}\right) B(\theta) \tag{27}$$

with

$$\mathcal{B} = \int_0^{\theta_\dagger} B(\theta) d\theta.$$

Then we have an endemic state, provided the threshold condition

$$\mathcal{R}_0 > 1$$

is satisfied. We note that both the *disease free* incidence and the *endemic* incidence

$$\sigma_* = \lambda_* S_* = \frac{N}{\mathcal{B}} \left(1 - \frac{1}{\mathcal{R}_0}\right)$$

are actually constant solutions of (24).

For the stability analysis of these states we rely on the linearization of the limiting equation (24) and on the analysis of the corresponding eigenvalue problem. Namely, linearizing (24) at the previous states we get

$$u(t) = \mathcal{R}_0 \int_0^\infty K_0(s) u(t-s) ds \tag{28}$$

for the disease free (26)and

$$u(t) = \int_0^\infty K_0(s) u(t-s) ds - (\mathcal{R}_0 - 1) \int_0^\infty K_1(s) u(t-s) ds \tag{29}$$

for the endemic one (with $\mathcal{R}_0 > 1$). Here we have set

$$K_0(t) = \frac{c(t)\chi(t)B(t)}{\int_0^{\theta_\dagger} c(t)\chi(t)B(t)dt}, \quad K_1(t) = \frac{B(t)}{\int_0^{\theta_\dagger} B(t)dt}. \tag{30}$$

These are normalized kernels such that $\widehat{K}_0(0) = \widehat{K}_1(0) = 1$. Furthermore, (28) and (29) respectively provide the characteristic equations

$$1 = \mathcal{R}_0 \widehat{K}_0(\lambda), \tag{31}$$

and

$$1 = \widehat{K}_0(\lambda) - (\mathcal{R}_0 - 1)\, \widehat{K}_1(\lambda) \tag{32}$$

Concerning (31) we have

Proposition 3 *Equation (31) has one and only one real solution α^* which is a simple root and*

i) $\alpha^* < 0$ *if and only if* $\mathcal{R}_0 < 1, \alpha^* = 0 if \mathcal{R}_0 = 1$
ii) *any other solution* α *of (31) is such that* $\Re\alpha < \alpha^*$,
iii) *within any strip* $\sigma_1 < \Re\lambda < \sigma_2$ *there is at most a finite number of roots of (31).*

Proof:

Consider the real function:

$$x \to \widehat{K}_0(x), \quad x \in \mathbf{R}. \tag{33}$$

Since $K_0(t) \geq 0$, this function is strictly decreasing and such that

$$\lim_{x \to -\infty} \widehat{K}_0(x) = +\infty, \quad \lim_{x \to +\infty} \widehat{K}_0(x) = 0.$$

Then, there is one and only one real solution α^* of (31) and, since

$$\left[\frac{d}{dx}\widehat{K}_0(x)\right]_{x=\alpha^*} = -\int_0^\infty t e^{-\alpha^* t} K_0(t)dt \; > \; 0,$$

α^* is simple. Of course $\alpha^* < 0$ if and only if $\mathcal{R}_0 = \mathcal{R}_0 \widehat{K}_0(0) =< 1$, while $\alpha^* = 0$ if $\mathcal{R}_0 = 1$.

Let α be a solution different from α^*. Then,

$$\int_0^\infty e^{-\alpha^* t} K_0(t)dt = \frac{1}{\mathcal{R}_0} = \Re\left(\int_0^\infty e^{-\alpha t} K_0(t)dt\right) =$$

$$= \int_0^\infty e^{-\Re\alpha\, t} cos(\Im\alpha\, t) K_0(t)dt \; < \; \int_0^\infty e^{-\Re\alpha\, t} K_0(t)dt$$

so that, since (33) is strictly decreasing, it follows that $\Re\alpha < \alpha^*$.

Finally, since $\widehat{K}_0(\lambda) \to 0$ as $|\lambda| \to +\infty$ in any half plane $\Re\lambda > \delta$, all the roots within the strip $\sigma_1 < \Re\lambda < \sigma_2$ must lie in some bounded subset and be finite in number because otherwise $\widehat{K}_0(\lambda)$, being analytical, would vanish identically. ∎

The previous Proposition shows that the disease free state is asymptotically stable as far as $\mathcal{R}_0 < 1$ and unstable if $\mathcal{R}_0 > 1$. Thus this state loses its stability

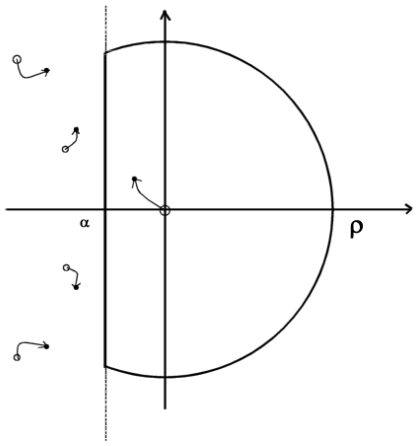

Figure 4: The roots of the characteristic equation (32) as $\mathcal{R}_0$ increases

at the critical value $\mathcal{R}_0 = 1$ i.e. at the critical value for the endemic state to

arise. Then we expect that the analysis of the characteristic equation (32) will show that this latter inherits the stability of the disease free one. Actually we have that this is certainly true if $\mathcal{R}_0$ is sufficiently close to 1.

Proposition 4 *There exists $\delta > 0$ such that if $0 < \mathcal{R}_0 - 1 < \delta$ then all the roots of (32) have negative real part.*

Proof:

We first recall (see the proof of the previous Proposition) that the equation

$$\widehat{K}_0(\lambda) = 1$$

has the real root $\lambda_0 = 0$ which is the unique one in the half plane $\Re\lambda \geq \alpha$ for some $\alpha \in (\beta, 0)$. Besides we set:

$$m = \inf_{y \in \mathbf{R}} \left| 1 - \hat{K}_0(\alpha + iy) \right| \; > \; 0$$

and take $L > 0$ such that

$$\frac{1}{2} < \left| 1 - \hat{K}_0(\lambda) \right| \qquad for \quad |\lambda| > L, \quad \Re\lambda \geq \alpha.$$

Then, if $\mathcal{R}_0 - 1 < \min\left\{m, \frac{1}{2}\right\}$ we have

$$\left| (\mathcal{R}_0 - 1)\, \widehat{K}_1(\lambda) \right| \; < \; \left| 1 - \hat{K}_0(\lambda) \right|$$

on the contour of any domain Σ_ρ such as that shown in Figure 4, with $\rho > L$. Consequently, by the Rouché theorem, equation (32) has one and only one root in the half plane $\Re\lambda \geq \alpha$.

In order to locate this root, let $\lambda(\mathcal{R}_0)$ be the differentiable path in the complex plane, originating from $\lambda(1) = 0$, such that $\lambda(\mathcal{R}_0)$ is a root of (32). Then from (32)

$$\frac{d}{d\mathcal{R}_0} \Re\left[\lambda(\mathcal{R}_0)\right] \Big|_{\mathcal{R}_0 = 1} = \; \frac{1}{\widehat{K}_1'(0)} < 0,$$

and we see that the path starting from $\lambda(1) = 0$ goes to the left of the imaginary axis as $\mathcal{R}_0$ increases from 1 (see Figure 4).

∎

As a matter of fact the location of the roots of (32) is not determined as $\mathcal{R}_0$ increases further. We may have different cases according to the shape of the kernels, including the occurrence of Hopf bifurcation. In fact we may envisage cases in which, as $\mathcal{R}_0$ increases, a couple of complex conjugate roots crosses the imaginary axis to the right so that the endemic state becomes unstable and a periodic solution is generated (this would lead to the bifurcation diagram of Figure 5). However the analysis of (**??**) in the general case is rather technical and not straightforward. We may discuss some significant examples and special conditions.

A first assumption concerns the kernel $K_1(t)$. In fact we have

Proposition 5 *Let $K_1(t)$ be two times differentiable, decreasing and convex. Then all the roots of (32) have negative real part for all $\mathcal{R}_0 > 1$.*

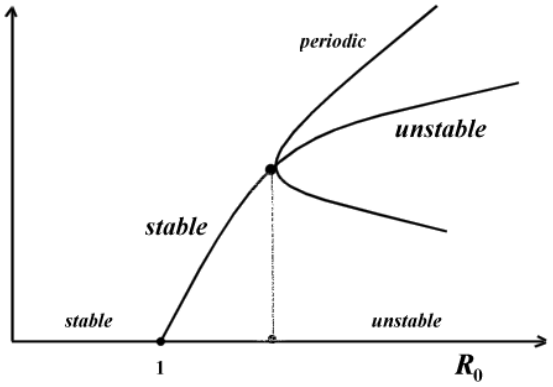

Figure 5: Bifurcation diagram

Proof:

First we note that $\lambda = 0$ cannot be a root because it implies $\mathcal{R}_0 = 1$. Then, since for $\mathcal{R}_0$ close to 1 all roots of (32) have negative real part, we contraddict the thesis assuming that there exists $\mathcal{R}_0^* > 1$ such that (32) has two immaginary roots $\lambda_\pm = \pm i\omega^*$ ($\omega^* > 0$). Then, using $K_1(\theta_\dagger) = K_1'(\theta_\dagger) = 0$ and integrating by parts, we have

$$\begin{aligned} 1 &= \int_0^{\theta_\dagger} K_0(s)\cos(\omega^* s)ds - (\mathcal{R}_0^* - 1)\int_0^{\theta_\dagger} K_1(s)\cos(\omega^* s)ds = \\ &= \int_0^{\theta_\dagger} K_0(s)\cos(\omega^* s)ds + \frac{(1-\mathcal{R}_0)}{\omega^{*2}}\int_0^{\theta_\dagger} K_1''(s)\left[1-\cos(\omega^* s)\right]ds \leq \\ &\leq \int_0^{\theta_\dagger} K_0(s)\cos(\omega^* s)ds < 1, \end{aligned}$$

which is a contradiction.

∎

Thus, in order to have sustained obscillations, we need $B(\theta)$ not to be regular and/or not convex. We may adopt the simple assumption that an infected stays infective with probability 1 until he recovers at the maximum age of infection $\theta_\dagger$

$$B(\theta) = 1 \quad for \quad \theta \in [0, \theta_\dagger].$$

This assumption leads to the following characteristic equation

$$1 = \widehat{K}_0(\lambda) + \frac{(1-\mathcal{R}_0)}{\theta_\dagger}\frac{1-e^{-\lambda\theta_\dagger}}{\lambda}. \tag{34}$$

Then we are left with assumptions on the kernel $K_0(\theta) = c(\theta)\chi(\theta)$, i. e. on the variable contact rate and infectiveness. In the simple case of constant contact rate and infectiveness equation (34) becomes

$$1 = \frac{(2-\mathcal{R}_0)}{\theta_\dagger}\frac{1-e^{-\lambda\theta_\dagger}}{\lambda}. \tag{35}$$

and the endemic state is stable for all $\mathcal{R}_0 > 1$ because there is no crossing of the imaginary axis. In fact if $\lambda = i\omega$ is a root of (35) this is equivalent to the system

$$1 - \cos(\omega\theta_\dagger) = 0$$
$$\frac{\theta_\dagger}{2 - \mathcal{R}_0} = \sin(\omega\theta_\dagger)$$

that has no solution. We note that with the assumptions above, equation (29) reduces to the following delay differntial equation

$$u'(t) = \frac{2 - \mathcal{R}_0}{\theta_\dagger} \left[u(t) - u(t - \theta_\dagger) \right].$$

The general case of variable contact rate and infectiveness is rather technical. In this respect equation (34) has been analized in [2], where the following main result is proven.

Theorem 4 *For each integer n such that the Fourier coefficient*

$$\int_0^{\theta_\dagger} K_0(s) \sin\left(\frac{2n\pi}{\theta_\dagger} s\right) ds > 0$$

there exists a value $\mathcal{R}_0^n$ at which (34) has a couple of imaginary roots $\lambda^n = \pm i\omega^n$ with $\omega^n \in [(2n-1)\pi, 2n\pi]$. These roots are simple and cross the imaginary axis from left to right as $\mathcal{R}_0$ increases crossing $\mathcal{R}_0^n$.

∎

Thus the simple S-I-S model is possibly very rich due to the age structure.

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