Global dynamics of a differential-difference system: A case of Kermack-McKendrick epidemic SIR model with age-structured protection phase

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Vaccination with temporary protection (duration τ)

$$
\begin{cases}
S'(t) &= \Lambda - \gamma S(t) - \beta S(t)I(t) - hS(t) + he^{-\gamma\tau}S(t-\tau), \\
I'(t) &= -\gamma I(t) + \beta S(t)I(t) - \mu I(t), \\
V'(t) &= -\gamma V(t) + hS(t) - he^{-\gamma\tau}S(t-\tau).
\end{cases}
$$

$\Lambda \Rightarrow$ Recruitment (births and immigration)
$\gamma \Rightarrow$ Mortality rate
$\beta \Rightarrow$ Contact rate per infective individual that result in infection
$h \Rightarrow$ Protection rate through for instance vaccination or drugs with temporary immunity
$\tau \Rightarrow$ Duration of the temporary protection phase
$\mu \Rightarrow$ Recovering rate (long-lasting immunity)

R. Xu, Appl. Math. Model. (2012) - Y. Kyrychko, K. Blyuss, Nonlinear Anal. (2005).

The disease-free equilibrium (DFE)

$$\left(\frac{\Lambda}{\gamma + h(1-e^{-\gamma\tau})}\ ,\ 0\ ,\ \frac{\Lambda h(1-e^{-\gamma\tau})}{\gamma(\gamma + h(1-e^{-\gamma\tau}))}\right).$$

The eradication condition

$$\tau > \frac{1}{\gamma}\ln\left(\frac{h}{h-\gamma(\mathcal{R}_0 - 1)}\right), \qquad \mathcal{R}_0 = \frac{\Lambda\beta}{\gamma(\mu+\gamma)} \quad (>1),$$

with $h > \gamma(\mathcal{R}_0 - 1)$. The eradication condition is equivalent to

$$h > \frac{\gamma(\mathcal{R}_0 - 1)}{1-e^{-\gamma\tau}}.$$

- The duration of protection provided by any mechanism plays an important role on the evolution and control of infectious diseases.
- It is sometimes difficult to reach a reasonable percentage of people to vaccinate in the total population.

Vaccination of newborns

$$\begin{cases} S'(t) &= (1-\alpha)\Lambda - \gamma S(t) - \beta I(t)S(t) - hS(t), \\ I'(t) &= -\gamma I(t) + \beta I(t)S(t) - \mu I(t), \\ V'(t) &= \alpha\Lambda - \gamma V(t) + hS(t), \qquad\qquad \tau = +\infty. \end{cases}$$

The disease-free equilibrium (DFE): $\left(\dfrac{(1-\alpha)\Lambda}{\gamma+h},\ 0\ ,\ \dfrac{(\alpha\gamma+h)\Lambda}{\gamma(\gamma+h)}\right).$

- The eradication condition, for the case $\alpha = 0$:

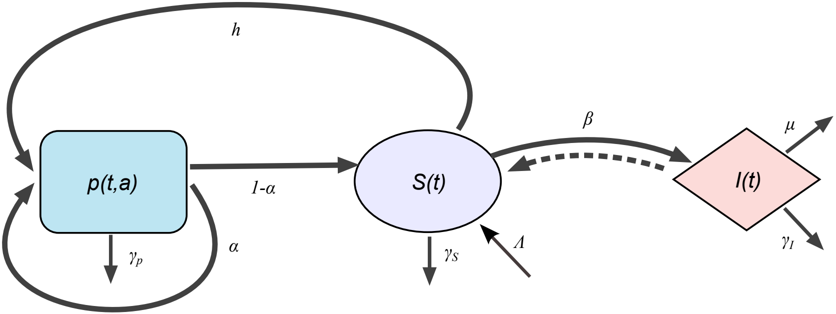
$$h > \gamma(\mathcal{R}_0 - 1), \qquad \mathcal{R}_0 := \frac{\beta}{\gamma+\mu} \quad (> 1).$$

- The eradication condition:

$$\alpha > 1 - \left(1 + \frac{h}{\gamma}\right)\frac{1}{\mathcal{R}_0} \qquad \text{in the case} \qquad h < \gamma(\mathcal{R}_0 - 1).$$

- Vaccination of newborns is an essential global strategy to stop some epidemics.
- The population of individuals that update their vaccine at the end of their period of protection has never been explicitly incorporated in the models.
- It would be interesting to combine vaccination of a part of total population with a proportion of individuals that were previously vaccinated.

SIR epidemic model with temprary protection phase



- $\gamma_S = \gamma_p = \gamma_I = \gamma$.
- $0 < \alpha < 1$: specific protection rate through for instance vaccination or drugs for individuals at the end of their period of protection.

The model is given by

$$\begin{cases} S'(t) &= \Lambda - \gamma S(t) - \beta S(t)I(t) - hS(t) + (1-\alpha)p(t,\tau), \\ I'(t) &= -\gamma I(t) + \beta S(t)I(t) - \mu I(t). \end{cases}$$

The evolution of the density of the protected individuals is given by

$$\frac{\partial}{\partial t}p(t,a) + \frac{\partial}{\partial a}p(t,a) = -\gamma p(t,a), \quad 0 < a < \tau.$$

The boundary condition ($a = 0$, $a = \tau$) is given by

$$p(t,0) = hS(t) + \alpha p(t,\tau).$$

We consider the total population of protected individuals

$$V(t) := \int_0^\tau p(t,a)da, \qquad t > 0.$$

$$\frac{\partial p}{\partial t} + \frac{\partial p}{\partial a} = -\gamma p,$$

Then, for $t > \tau$, we have

$$p(t,\tau) = e^{-\gamma\tau} p(t-\tau, 0).$$

In another side, by integrating over the age variable we obtain

$$\begin{cases} S'(t) &= \Lambda - \gamma S(t) - \beta S(t) I(t) - hS(t) + (1-\alpha) p(t,\tau), \\ I'(t) &= -\gamma I(t) + \beta S(t) I(t) - \mu I(t), \\ V'(t) &= -\gamma V(t) + hS(t) - (1-\alpha) p(t,\tau), \\ p(t,0) &= hS(t) + \alpha p(t,\tau), \end{cases}$$

where

$$V(t) := \int_0^\tau p(t,a)da \quad \text{and} \quad p(t,\tau) = e^{-\gamma\tau} p(t-\tau, 0).$$

We put

$$v(t) := p(t,0), \quad t > \tau.$$

Then, the system becomes

$$\begin{cases} S'(t) &= \Lambda - \gamma S(t) - \beta S(t)I(t) - hS(t) + (1-\alpha)e^{-\gamma\tau}v(t-\tau), \\ I'(t) &= -\gamma I(t) + \beta S(t)I(t) - \mu I(t), \\ V'(t) &= -\gamma V(t) + hS(t) - (1-\alpha)e^{-\gamma\tau}v(t-\tau), \\ v(t) &= hS(t) + \alpha e^{-\gamma\tau}v(t-\tau). \end{cases}$$

We focus on the system

$$\begin{cases} S'(t) &= \Lambda - \gamma S(t) - \beta S(t)I(t) - hS(t) + (1-\alpha)e^{-\gamma\tau}v(t-\tau), \\ I'(t) &= -\gamma I(t) + \beta S(t)I(t) - \mu I(t), \\ v(t) &= hS(t) + \alpha e^{-\gamma\tau}v(t-\tau). \end{cases}$$

The basic reproduction number $\mathcal{R}_0$

$$\begin{cases} S'(t) & = & \Lambda - \gamma S(t) - \beta S(t)I(t) - hS(t) + (1-\alpha)e^{-\gamma\tau}v(t-\tau), \\ I'(t) & = & -\gamma I(t) + \beta S(t)I(t) - \mu I(t), \\ v(t) & = & hS(t) + \alpha e^{-\gamma\tau}v(t-\tau). \end{cases}$$

The number $\mathcal{R}_0$ is defined as the average number of secondary infections that occur when one infective individual is introduced into a completely susceptible population. We have from the system

$$\frac{I'(t)}{(\mu+\gamma)I(t)} = -1 + \frac{\beta}{\mu+\gamma}S(t).$$

The fraction $\beta/(\mu+\gamma)$ can be interpreted as the number of contacts per infected individual during his infectious period that leads to the transmission of the disease.

If $\quad \dfrac{\beta}{\mu+\gamma} S(t) > 1, \quad$ the disease persist, otherwise, it disappears.

At the disease-free equilibrium (DFE), $(S^0, 0, v^0)$, given by

$$\left(\frac{\Lambda(1-\alpha e^{-\gamma\tau})}{\gamma + h - (\alpha\gamma + h)e^{-\gamma\tau}} \ , \ 0 \ , \ \frac{\Lambda h}{\gamma + h - (\alpha\gamma + h)e^{-\gamma\tau}} \right),$$

the basic reproduction number is defined by

$$\frac{\beta}{\mu+\gamma} S^0 = \frac{\beta}{\mu+\gamma} \times \frac{\Lambda(1-\alpha e^{-\gamma\tau})}{\gamma + h - (\alpha\gamma + h)e^{-\gamma\tau}}.$$

Suppose that

$$h < \frac{\gamma(\mathcal{R}_0 - 1)}{1 - e^{-\gamma\tau}} \quad \text{with} \quad \mathcal{R}_0 = \frac{\Lambda\beta}{\gamma(\mu+\gamma)}.$$

The eradication condition (to prove):

$$\alpha > \frac{\gamma(\mathcal{R}_0 - 1) - h(1 - e^{-\gamma\tau})}{\gamma e^{-\gamma\tau}(\mathcal{R}_0 - 1)}.$$

Analysis of the differential-difference system

$$\begin{cases} S'(t) &= \Lambda - \gamma S(t) - \beta S(t)I(t) - hS(t) + (1-\alpha)e^{-\gamma\tau}v(t-\tau), \\ I'(t) &= -\gamma I(t) + \beta S(t)I(t) - \mu I(t), \\ v(t) &= hS(t) + \alpha e^{-\gamma\tau}v(t-\tau). \end{cases}$$

A general form (it could be compared to a neutral delay differential system, under a compatibility condition)

$$\begin{cases} x'(t) &= -f(x(t)) + \sum_{j=1}^{n} A_j w(t-\tau_j), \\ w(t) &= g(x(t)) + \sum_{j=1}^{n} B_j w(t-\tau_j). \end{cases}$$

Eigenvalues coming from infinity

$$\begin{cases} y'(t) & = & -v(t), \\ v(t) & = & y(t) - 2v(t-\tau), \end{cases}$$

For $\tau = 0$, we have

$$\begin{cases} y'(t) & = & -\frac{1}{3}y(t) & \Rightarrow & y(t) = y_0 e^{-t/3} \\ v(t) & = & \frac{1}{3}y(t) & \Rightarrow & v(t) = \frac{y_0}{3} e^{-t/3}. \end{cases}$$

But for $\tau > 0$, the trivial solution of

$$\begin{cases} y'(t) & = & -v(t), \\ v(t) & = & y(t) - 2v(t-\tau), \end{cases}$$

is unstable (see the proof).

Proof

The characteristic equation

$$\Delta(\lambda) := \lambda \left(1 + 2e^{-\tau\lambda}\right) + 1 = 0,$$

which is equivalent to

$$\Delta(\lambda) := e^{\tau\lambda} \left(1 + \frac{1}{\lambda}\right) + 2 = 0.$$

If $\{\lambda_n\}$ is a sequence of distinct roots of Δ, then

$$\lim_{n\to+\infty} |\lambda_n| = +\infty \qquad \text{and} \qquad \lim_{n\to+\infty} (e^{\tau\lambda_n} + 2) = 0.$$

The roots of $e^{\tau\lambda} + 2 = 0$ are

$$\lambda'_k = \frac{\ln(2)}{\tau} + \frac{2k\pi i}{\tau}, \qquad k = 0, \pm1, \pm2, \cdots .$$

There exist sub-sequences of λ_n and λ'_k such that

$$\lambda_j - \lambda'_j \to 0 \qquad \text{as} \qquad j \to +\infty.$$

Fundamental result

$$\begin{cases} y'(t) & = & ay(t) + \beta v(t-\tau), \\ v(t) & = & by(t) + \alpha v(t-\tau). \end{cases}$$

The characteristic equation

$$e^{\tau\lambda}\left(1 - \frac{a}{\lambda}\right) - \alpha - \frac{b\beta - a\alpha}{\lambda} = 0.$$

Theorem

If $|\alpha| < 1$ and every solution for $\tau = 0$ approaches zero, then there is $\tau_0 > 0$ such that every solution approaches zero for $0 \leq \tau < \tau_0$.

L.A.S of the disease-free steady state ($\mathcal{R}_0 < 1$)

- The linearized system about the equilibrium $(S^0, 0, v^0)$ is given by

$$\begin{cases} S'(t) &= -(\gamma+h)S(t) - \beta S^0 I(t) + (1-\alpha)e^{-\gamma\tau}v(t-\tau), \\ I'(t) &= -(\mu+\gamma)I(t) + \beta S^0 I(t), \\ v(t) &= hS(t) + \alpha e^{-\gamma\tau}v(t-\tau). \end{cases}$$

The characteristic equation of this system is given for $\lambda \in \mathbb{C}$, by

$$\begin{aligned} \Delta(\tau,\lambda) &= \left(\lambda+\mu+\gamma-\beta S^0\right) \times \\ &\quad \left[\lambda+\gamma+h-\left(\alpha(\lambda+\gamma+h)e^{-\gamma\tau}+h(1-\alpha)e^{-\gamma\tau}\right)e^{-\lambda\tau}\right], \\ &= 0. \end{aligned}$$

From the characteristic equation, we have the following eigenvalue

$$\lambda = -\mu-\gamma+\beta S^0 = (\mu+\gamma)(\mathcal{R}_0-1) < 0.$$

$$e^{\lambda\tau}\left(1+\frac{\gamma+h}{\lambda}\right)-\alpha e^{-\gamma\tau}-\frac{\alpha\gamma+h}{\lambda}e^{-\gamma\tau}=0.$$

For $\tau=0$,

$$(1-\alpha)\left(1+\frac{\gamma}{\lambda}\right)=0.$$

There exists only one root given by $\lambda=-\gamma<0$.
We have

$$0<\alpha e^{-\gamma\tau}<1.$$

We look for purely imaginary roots $\pm i\omega,\quad \omega>0.$ We put

$$\eta=\alpha e^{-\gamma\tau}<1 \qquad \text{and} \qquad \rho=\alpha(\gamma+h)e^{-\gamma\tau}+h(1-\alpha)e^{-\gamma\tau}>0.$$

Then, by separating real and imaginary parts, we obtain

$$\begin{cases} \cos(\omega\tau) & = & \dfrac{\omega^2\eta+(\gamma+h)\rho}{\rho^2+(\eta\omega)^2}, \\[2ex] \sin(\omega\tau) & = & \dfrac{\omega(\rho-(\gamma+h)\eta)}{\rho^2+(\eta\omega)^2}. \end{cases}$$

It follows, by taking $\cos^2(\omega\tau) + \sin^2(\omega\tau) = 1$, that

$$\omega^2 = \frac{\rho^2 - (\gamma + h)^2}{1 - \eta^2} = \frac{(\rho - (\gamma + h))(\rho + (\gamma + h))}{(1 - \eta)(1 + \eta)}.$$

We can observe that $\rho - (\gamma + h) < 0$ which is absurd.

Then, no $i\omega$ satisfying the characteristic equation exist.

Hence, when $\mathcal{R}_0 < 1$ all roots of the characteristic equation have negative real parts.

- If $\mathcal{R}_0 < 1$ the steady state $(S^0, 0, v^0)$ is L.A.S.
- If $\mathcal{R}_0 > 1$ the steady state $(S^0, 0, v^0)$ is unstable.

Lyapunov functional and global asymptotic stability (GAS)

GAS of the disease-free steady state ($\mathcal{R}_0 < 1$)

We prove the global asymptotic stability of the disease-free steady state $(S^0, 0, v^0)$ of the system

$$\begin{cases} S'(t) &= \Lambda - (\gamma + h)S(t) - \beta S(t)I(t) + (1-\alpha)e^{-\gamma\tau}v(t-\tau), \\ I'(t) &= -(\mu+\gamma)I(t) + \beta S(t)I(t), \\ v(t) &= hS(t) + \alpha e^{-\gamma\tau}v(t-\tau). \end{cases}$$

From the difference equation

$$v(t) = hS(t) + \alpha e^{-\gamma\tau} v(t-\tau), \qquad v(t) = \phi(t), \;\; t \in [-\tau, 0],$$

we obtain the existence of constants $C > 0$ and $\sigma > 0$ such that

$$|v(t)| \leq C \left[\|\phi\| e^{-\sigma t} + \sup_{0 \leq s \leq t} |S(s)| \right].$$

The solutions of the system

$$\begin{cases} S'(t) &= \Lambda - (\gamma + h)S(t) - \beta S(t)I(t) + (1-\alpha)e^{-\gamma\tau} v(t-\tau), \\ I'(t) &= -(\mu + \gamma)I(t) + \beta S(t)I(t), \\ v(t) &= hS(t) + \alpha e^{-\gamma\tau} v(t-\tau), \end{cases}$$

satisfy, for all $t > 0$,

$$\begin{cases} S'(t) & \leq & \Lambda - (\gamma + h)S(t) + (1-\alpha)e^{-\gamma\tau}u(t-\tau), \\ u(t) & = & hS(t) + \alpha e^{-\gamma\tau}u(t-\tau). \end{cases}$$

By the comparison principle, we have $S(t) \leq S^+(t)$ and $u(t) \leq u^+(t)$ for all $t > 0$, where (S^+, u^+) is the solution of the following problem

$$\begin{cases} \dfrac{dS^+(t)}{dt} = \Lambda - (\gamma + h)S^+(t) + (1-\alpha)e^{-\gamma\tau}u^+(t-\tau), \\ u^+(t) = hS^+(t) + \alpha e^{-\gamma\tau}u^+(t-\tau), \\ \\ S^+(0) = S_0, \quad u^+(s) = \phi(s), \quad \text{for} \quad -\tau \leq s \leq 0. \end{cases}$$

This system has a unique steady state (S^0, u^0), where S^0 and u^0 are the first and third components of the disease-free steady state of the main system.

We put, for $t > 0$,

$$\begin{cases} \hat{S}(t) = S(t) - S^0, \\ \hat{u}(t) = u(t) - u^0. \end{cases}$$

Then, we get the linear differential-difference system

$$\begin{cases} \hat{S}'(t) & = & -(\gamma_S + h)\hat{S}(t) + (1-\alpha)e^{-\gamma\tau}\hat{u}(t-\tau), \\ \hat{u}(t) & = & h\hat{S}(t) + \alpha e^{-\gamma\tau}\hat{u}(t-\tau). \end{cases}$$

We consider the following Lyapunov functional

$$\begin{array}{rccc} V: & \mathbb{R}^+ \times C^+ & \to & \mathbb{R}^+, \\ & (S_0, \phi) & \mapsto & V(S_0, \phi), \end{array}$$

defined by

$$V(S_0, \phi) = \frac{S_0^2}{2} + \vartheta \int_{-\tau}^{0} \phi^2(\theta) d\theta \qquad \text{with} \quad \vartheta = \frac{\gamma(1 - (\alpha e^{-\gamma\tau})^2) + h}{2h^2}.$$

Moreover, the system is input-to-state stable: There exist constants $C > 0$ and $\sigma > 0$ such that the solution $(\hat{S}, \hat{u})$ satisfies

$$|\hat{u}(t)| \leq C \left[\|\phi\| e^{-\sigma t} + \sup_{0 \leq s \leq t} |\hat{S}(s)| \right].$$

Hence $(0, 0)$ is a globally asymptotically stable steady state of

$$\begin{cases} \hat{S}'(t) & = & -(\gamma_S + h)\hat{S}(t) + (1-\alpha)e^{-\gamma\tau}\hat{u}(t-\tau), \\ \hat{u}(t) & = & h\hat{S}(t) + \alpha e^{-\gamma\tau}\hat{u}(t-\tau). \end{cases}$$

Let $\epsilon > 0$ and consider the set

$$\Omega_\epsilon := \big\{ (S, I, u) \in \mathbb{R}^+ \times \mathbb{R}^+ \times C^+ : 0 \leq S \leq S^0 + \epsilon \ \text{ and } \\ 0 \leq u(s) \leq u^0 + \epsilon, \ \text{ for all } s \in [-\tau, 0] \big\} .$$

For sufficiently small $\epsilon > 0$, the subset Ω_ϵ of $\mathbb{R}^+ \times \mathbb{R}^+ \times C^+$ is a global attractor for the last system.

We can restrict the global stability analysis of the disease-free steady state of the main system to the set Ω_ϵ.

Theorem

Assume that $\mathcal{R}_0 < 1$. Then, the disease-free steady state $(S^0, 0, u^0)$ of the main system is globally asymptotically stable.

Endemic steady state $(\overline{S}, \overline{I}, \overline{v})$

$$\mathcal{R}_0 = \frac{\Lambda\beta(1-\alpha e^{-\gamma\tau})}{(\mu+\gamma)(\gamma+h-(\alpha\gamma+h)e^{-\gamma\tau})} > 1.$$

The disease-free steady state $(S^0, 0, v^0)$ is unstable, because we have the following eigenvalue

$$\lambda = (\mu+\gamma)(\mathcal{R}_0 - 1) > 0.$$

There exists a unique endemic steady state

$$(\overline{S}, \overline{I}, \overline{v}) = \left(\frac{\mu+\gamma}{\beta} \ , \ \frac{\Lambda}{\mu+\gamma}\left(1-\frac{1}{\mathcal{R}_0}\right) \ , \ \frac{h(\mu+\gamma)}{\beta(1-\alpha e^{-\gamma\tau})}\right).$$

The GAS of the endemic steady state $(\overline{S}, \overline{I}, \overline{v})$

We put $\tilde{S}(t) := S(t) - \overline{S}$ and $\tilde{v}(t) := v(t) - \overline{v}$.
Then,

$$\begin{cases} \tilde{S}'(t) & = & -(\gamma + h)\tilde{S}(t) - \beta\tilde{S}(t)I(t) - \beta\overline{S}I(t) + \beta\overline{S}\,\overline{I} \\ & & +(1-\alpha)e^{-\gamma\tau}\tilde{v}(t-\tau), \\ I'(t) & = & \beta\tilde{S}(t)I(t), \\ \tilde{v}(t) & = & h\tilde{S}(t) + \alpha e^{-\gamma\tau}\tilde{v}(t-\tau). \end{cases}$$

We consider the Lyapunov function

$$W(t) = \frac{\tilde{S}(t)^2}{2} + K\int_{t-\tau}^{t} \tilde{v}^2(\sigma)d\sigma + \overline{S}\left(I(t) - \overline{I} - \overline{I}\ln\left(\frac{I(t)}{\overline{I}}\right)\right),$$

where

$$K = \frac{\gamma(1 - (\alpha e^{-\gamma\tau})^2) + h}{2h^2}.$$

Conclusion

$$\begin{cases} S'(t) = \Lambda - \gamma S(t) - hS(t) - \beta S(t)I(t) + (1-\alpha)p(t,\tau), \\ I'(t) = -\gamma I(t) - \mu I(t) + \beta S(t)I(t), \\ \dfrac{\partial}{\partial t}p(t,a) + \dfrac{\partial}{\partial a}p(t,a) = -\gamma p(t,a), \qquad 0 < a < \tau, \\ p(t,0) = hS(t) + \alpha p(t,\tau). \end{cases}$$

- If
$$\alpha > \frac{\gamma(\mathcal{R}_0 - 1) - h(1 - e^{-\gamma\tau})}{\gamma e^{-\gamma\tau}(\mathcal{R}_0 - 1)}, \quad \text{with} \quad \mathcal{R}_0 = \frac{\Lambda\beta}{\gamma(\mu+\gamma)},$$
the disease-free equilibrium is G.A.S.
- If $\alpha < \dfrac{\gamma(\mathcal{R}_0 - 1) - h(1 - e^{-\gamma\tau})}{\gamma e^{-\gamma\tau}(\mathcal{R}_0 - 1)}$, the endemic steady state is G.A.S.

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Thank you

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