Доклади на Българската академия на науките Comptes rendus de l'Académie bulgare des Sciences

Tome 69, No 7, 2016

MATHEMATIQUES

Modèles mathématiques

EPIDEMIC DYNAMICS OF AN INFECTION THROUGH THE PATHOGEN DENSITY IN THE ENVIRONMENT

Begoña Cantó, Carmen Coll, Elena Sánchez

(Submitted by Academician P. Popivanov on February 24, 2016)

Abstract

We propose a mathematical model for the indirect transmission via a contaminated environment by a disease agent and we analyze the possibility that the initial infection can spread in the population. We have used the significance of the basic reproduction number, since the disease-free state is either stable or unstable depending on its value, to obtain an explicit expression for R_0 . This expression is found to give threshold conditions for the stability of the disease-free equilibrium or the existence of an endemic equilibrium in a population.

Key words: epidemic models, basic reproduction number, stability, disease-free equilibrium point, Endemic equilibrium point

2000 Mathematics Subject Classification: 92B99, 93D20

This research was partially supported by Ministerio de Economia y Competitividad under grant MTM2013-43678-P.

1. Introduction. Differential or difference equations have been widely used to describe the behaviour of demographic, biological or chemical processes, $[^{1-3}]$, as well as their properties of stability, controllability, optimization, etc., see for instance $[^4]$.

In recent years, mathematical epidemic models that represent the dynamic of diseases that are directly transmitted between individuals have been studied in the literature. Mathematical aspects such as existence of solutions, existence of disease-free and endemic equilibrium points, stability, and thresholds have been analyzed for several authors (see, for example [5-8]).

We are interested in the design of a mathematical model which analyzes diseases whose transmission occurs through a contaminated environment. We assume that the disease spreads due to a certain bacteria or virus found in the environment or that is present in food, like salmonellosis. Some results on Salmonella in industrial house hens can be found in [9,10].

In this paper, we develop a mathematical model with a set of difference equations where the variables S(t) and I(t) represent time dependent population densities rather of susceptible and infected individuals at time $t, t \in \mathbb{Z}, t \geq 0$. We are interested in achieving a good understanding of the spread of infectious diseases taking into account the population size. To this end, a population threshold has been investigated for the analysis of the epidemic process taking into account the pathogen density in the environment. In our model, the variable C(t) represents the environmental contamination at time $t, t \in \mathbb{Z}, t \geq 0$, that is, for example, pathogen load in the environment. We assume that the population has constant size N. Furthermore, the parameters 0 < p, q, s < 1 shall represent density survival rate of S(t), I(t) and C(t), respectively, and the death removal rate at time t is denoted by $\mu(t)$. Transmission via contact with the contaminated environment is given by $\sigma C(t)S(t)$ where σ denotes the exposition rate. For different values of this parameter we can get different types of infections.

Then, the model is described by the following nonlinear system:

$$\begin{array}{lcl} S(t+1) & = & pS(t) - \sigma C(t)S(t) + \mu(t)N \\ I(t+1) & = & qI(t) + \sigma C(t)S(t) \\ C(t+1) & = & sC(t) + \beta I(t), \ t \geq 0, \ t \in \mathbb{Z}. \end{array}$$

In the above system, the term $\mu(t)N$ and the term $\beta I(t)$, $0 < \beta < 1$, represent the replacement rate and the density of pathogen produced by individuals infected, respectively. It can obtain the parameter $\mu(t)$ in terms of the susceptible population by considering two basic assumptions for these models: each individual has the same probability of catching the disease and the total population size remains

constant, ie, S(t) + I(t) = N, $\forall t \geq 0$. Then, the system is

$$S(t+1) = qS(t) - \sigma C(t)S(t) + (1-q)N$$

$$I(t+1) = qI(t) + \sigma C(t)S(t)$$

$$C(t+1) = sC(t) + \beta I(t).$$

Since all variables and parameters that appear in the above system are non-negative, to ensure that the system (1) has nonnegative solution, we only need to look at the equation $S(t+1) = (q - \sigma C(t))S(t) + (1-q)N \ge 0, \forall t \ge 0$. Thus, a sufficient condition to have a nonnegative solution is $C(t) \le \frac{q}{\sigma}$.

Furthermore, from zero initial condition C(0) = 0, we obtain the maximum number of bacteria which would be bounded by $\frac{\beta N}{1-s}$. This last statement follows directly from considering the equation $C(t+1) = sC(t) + \beta I(t)$ of the system (1) for $t=0,1,\ldots$ and given that the total number of infected satisfies $I(t) \leq N$, then we obtain

$$C(t) = s^t C(0) + \beta \sum_{i=0}^{t-1} s^i I(i) \le s^t C(0) + \beta N \sum_{i=0}^{t-1} s^i. \quad C(0) = 0 \implies C(t) \le \frac{\beta N}{1-s}.$$

To analyze the behaviour of this model the idea is to approximate the non-linear system by a linear one (around the equilibrium point) in the next section we obtain the equilibrium points.

2. Equilibrium points. The equilibrium points (S^*, I^*, C^*) are the solutions of the following equations:

$$S^* = qS^* - \sigma C^*S^* + (1 - q)N$$

 $I^* = qI^* + \sigma C^*S^*$
 $C^* = sC^* + \beta I^*$.

If $I^* = 0$, we obtain a disease-free equilibrium point, $P_f = (S_f, 0, 0)$ where $S_f = N$; otherwise, we find the endemic equilibrium point, $P_e = (S_e, I_e, C_e)$. The way to obtain the equilibrium points proves their existence and uniqueness. On the existence of the equilibrium point we have the following result.

Proposition 1. Consider model (1).

- a) This model always has a disease-free equilibrium $P_f = (N, 0, 0)$.
- b) If $S_e = \frac{(1-q)(1-s)}{\sigma\beta} < N$, model (1) has also a unique endemic equilibrium $P_e = \left(S_e, N S_e, (N S_e) \frac{\beta}{1-s}\right)$.

Note that to ensure the existence of the endemic equilibrium point we have to consider the size of the population N greater than $K = \frac{(1-q)(1-s)}{\sigma\beta}$, otherwise the pathogen density C_e will be negative which is meaningless.

The behaviour of the system solution in a neighborhood of an equilibrium point, i.e., whether it is stable or not, allows us to deduce whether the disease will disappear, will be endemic or it grows creating a pandemic. The next section shows that the stability analysis of solutions of our model relies on the stability analysis of a linear difference system.

2.1. The disease-free equilibrium point. Assume that P_f is an equilibrium point. Then $S(t)C(t) \simeq NC(t)$. Denote $\hat{S} = S(t) - N$, $\hat{I} = I(t)$, $\hat{C} = C(t)$.

To analyze the behaviour of the solution around the P_f , we consider the subsystem given by

$$\hat{x}(t+1) = A\hat{x}(t)$$
 with $\hat{x}(t) = \begin{pmatrix} \hat{I}(t) \\ \hat{C}(t) \end{pmatrix}$ and $A = \begin{pmatrix} q & \sigma N \\ \beta & s \end{pmatrix}$

and we study if this system is asymptotically stable to the disease-free equilibrium, i.e. whether $\rho(A) < 1$, where $\rho(\cdot)$ denotes the spectral radius of a matrix. From the literature this property is also referred to as Schur stable matrix or convergent matrix.

The coefficient matrix A can be written using the Transition matrix, denoted by T and the Fertility matrix, denoted by F as follows:

$$A = T + F = \left(\begin{array}{cc} q & 0 \\ 0 & s \end{array} \right) + \left(\begin{array}{cc} 0 & \sigma N \\ \beta & 0 \end{array} \right).$$

One of the most important parameters of epidemic modelling is the basic reproduction number \mathcal{R}_0 which is a measure or indicator to know whether the disease will disappear at all or not. We shall study the stability property using \mathcal{R}_0 ,

$$\mathcal{R}_0 = \rho(F(I-T)^{-1}) = \sqrt{\frac{\beta \sigma N}{(1-q)(1-s)}}.$$

This parameter represents an epidemic threshold and it is possible to describe the behaviour of the system using the value of \mathcal{R}_0 . The disease-free equilibrium is asymptotically stable when $\mathcal{R}_0 < 1$, in this case, the disease will die out in the long run. But, if $\mathcal{R}_0 > 1$, then the disease will be able to spread through a population. The next result describes the different behaviours of the system with respect to the basic reproduction number and it follows directly from the definition of \mathcal{R}_0 .

Proposition 2. Consider the epidemic model given in (1).

(i) If N < K then $\mathcal{R}_0 < 1$ and the infection cannot persist.

(ii) If N > K then $\mathcal{R}_0 > 1$ and P_e is positive. In this case, the infection persists or spreads.

Furthermore, note that, if 0 < N < K and $C(t) \le \frac{q}{\sigma}$, then in the long run $0 < \sigma C(t) < \frac{\beta \sigma}{1-s} N < q < 1$.

2.2. The endemic equilibrium point. In this part, we mainly analyze the permanence of the infection. To get this we consider that $S(t)C(t) \simeq S_eC_e + S_e(C(t) - C_e) + C_e(S(t) - S_e)$. Denote $\hat{S} = S - S_e$, $\hat{I} = I - I_e$, $\hat{C} = C - C_e$ and a closed-loop system to the original nonlinear system is

$$\hat{x}(t+1) = \hat{A}\hat{x}(t)$$

with
$$\hat{x}(t) = (\hat{S}(t) \ \hat{I}(t) \ \hat{C}(t))^T$$
 and $\hat{A} = \begin{pmatrix} q - \sigma C_e & 0 & -\sigma S_e \\ \sigma C_e & q & \sigma S_e \\ 0 & \beta & s \end{pmatrix}$.

It is clear that if the spectral radius of matrix \hat{A} is less than 1, the system is asymptotically stable and $\hat{x_e} = \lim_{t\to\infty} \hat{A}^t \hat{x_0} = 0$ for all nonnegative initial conditions. In this case, the permanent infection is endemic and it tends to the point P_e . In the next results we obtain conditions on its eigenvalues.

Proposition 3. All eigenvalues of \hat{A} are real.

Proof. The solution of the algebraic equation $|\lambda I - \hat{A}| = 0$ are $\lambda = q$ and $D = (s + q - \sigma C_e)^2 + 4(1 + s\sigma C_e - (q + s))$ is the discriminant. We construct the parabola $f(\lambda) = \lambda^2 + \lambda(4s - 2(s + q)) + (s + q)^2 + 4(1 - (q + s))$, and it is easy to check that $D = f(\sigma C_e)$. The above function $f(\lambda)$ has a minimum in $\lambda = q - s$ and f(q - s) = 4(1 - q)(1 - s) > 0. Thus, $f(\lambda) > 0$ for all λ , in particular $D = f(\sigma C_e) > 0$, then all eigenvalues of \hat{A} are real.

In the following result we seek conditions to determine the sign of the eigenvalues. Note that the size of the population plays an important role in these results.

Proposition 4.

- 1. If $q + s \le 1$, then \hat{A} has two positive and one negative eigenvalues.
- 2. If q + s > 1 and $\alpha = 1 + \frac{q + s 1}{s(1 q)}$, then
 - (a) If $K < N < \alpha K$, then all eigenvalues of \hat{A} are positive.
 - (b) If $N > \alpha K$, then \hat{A} has two positive and one negative eigenvalues.

Proof. 1. Suppose $q+s \leq 1$. Then, $1-(q+s)+s\sigma C_e>0$ and D>0. Thus, $|q+s-\sigma C_e|<\sqrt{D}$ and only $\lambda=\frac{1}{2}(s+q-\sigma C_e-\sqrt{D})$ is negative. Hence, \hat{A} has two positive and one negative eigenvalues.

2. Suppose q + s > 1, then

(a) Assume
$$K < N < \alpha K$$
. Since $(\frac{1}{1-q} - \frac{1-s}{s}) < \frac{s+1}{1-q}$ then $N < \frac{s+1}{1-q}K$, that is $\frac{(1-q)N}{K} < s+1$.

Now, we study the sign of $s + q - \sigma C_e$ and the sign of $(1 - (q + s) + s\sigma C_e)$. From $C_e = \frac{\beta}{1 - s}(N - K) > 0$ we observe that $s + q - \sigma C_e = s + 1 - \frac{(1 - q)N}{K} > 0$. Moreover, as $K < N < \alpha K$,

$$(1 - (q + s) + s\sigma C_e) = s\left((1 - \alpha)(1 - q) + \frac{\sigma\beta}{1 - s}(N - K)\right) < 0.$$

That is, $(s + q - \sigma C_e)^2 > D^2$,

 $\lambda_{1,2} = \frac{1}{2}(s+q-\sigma C_e \pm \sqrt{D})$. Then, all of the eigenvalues of \hat{A} , $\lambda_0 = q$ and $\lambda_{1,2} = \frac{1}{2}(s+q-\sigma C_e \pm \sqrt{D})$ are positive.

(b) Suppose $N > \alpha K$. Using the definition of C_e , in a similar way as above we obtain $(s + q - \sigma C_e)^2 < D^2$. Thus $\lambda = \frac{1}{2}(s + q - \sigma C_e + \sqrt{D})$ is positive and $\lambda = \frac{1}{2}(s + q - \sigma C_e - \sqrt{D})$ is negative. Hence, \hat{A} has two positive eigenvalues and one negative.

In the following lemmas we analyze when the eigenvalues of \hat{A} are inside of the unit circle, i.e., $|\lambda| < 1$.

Lemma 1. For any population of size N, if \hat{A} has a positive eigenvalue λ_0 then $0 < \lambda_0 < 1$.

Proof. Suppose $\lambda_0 > 0$ is a real eigenvalue of \hat{A} . We distinguish two cases 1. If $\lambda_0 > q - \sigma \frac{C_e}{2}$, then $2(\lambda_0 - q) + \sigma C_e > 0$ and $(\lambda_0 - q)^2 + 2(\lambda_0 - q)\sigma C_e + \sigma^2 C_e^2 > (\lambda_0 - q)^2$. Thus, we have $(\lambda_0 - q + \sigma C_e)^2 > (\lambda_0 - q)^2$. Since λ_0 is an eigenvalue of \hat{A} , then $(\lambda_0 - q + \sigma C_e)(\lambda_0 - q)(\lambda_0 - s) - (\lambda_0 - q)(1 - q)(1 - s) = 0$ and

$$\left| \frac{(\lambda_0 - q)(\lambda_0 - s)}{(1 - q)(1 - s)} \right| = \left| \frac{(\lambda_0 - q)}{(\lambda_0 - q + \sigma C_e)} \right| < 1.$$

So, $-(1-q)(1-s) < (\lambda_0-q)(\lambda_0-s) < (1-q)(1-s)$ and then $\lambda_0^2 - (q+s)\lambda_0 + (q+s) - 1 < 0$. Construct the polynomial function $p(\lambda) = \lambda^2 - (q+s)\lambda + (q+s) - 1$ whose graph is an upwards opened parabola, which minimum is reached when $\lambda = \frac{q+s}{2}$.

Since $p(\lambda_0) < 0$, the roots $\lambda_1 = q + s - 1$ and $\lambda_2 = 1$ of $p(\lambda) = 0$ satisfy $\lambda_1 < \lambda_0 < \lambda_2$. Since 0 < q, s < 1, then -1 < q + s - 1 < 1 and λ_0 satisfies $-1 < q + s - 1 < \lambda_0 < 1$, that is, $|\lambda_0| < 1$.

2. If $\lambda_0 < q - \sigma \frac{C_e}{2}$ using 0 < q < 1 and $\sigma \frac{C_e}{2} > 0$, we have $q - \sigma \frac{C_e}{2} < 1$.

Then, $0 < \lambda_0 < q - \sigma \frac{\bar{C}_e}{2} < 1$.

Then, the eigenvalues satisfy $0 < \lambda_0 < 1$.

From now on, we denote $\theta = 1 + \frac{2(q+s)}{(1-q)(s+1)}$. In the next results θ will be a bound that determines the convergence of the model to P_e .

Lemma 2. Consider the size of the population N such that $K < N < \theta K$. If A has one negative eigenvalue λ then $|\lambda| < 1$.

Proof. From Proposition 4 if \hat{A} has one negative eigenvalue, we only need to check that $\lambda = \frac{1}{2}(s + q - \sigma C_e - \sqrt{D}) > -1$.

Using the parameters K and C_e we have $s+q-\sigma C_e>s\sigma C_e-(q+s)$. Then, $D<(s+q-\sigma C_e+2)^2$, and $-2< s+q-\sigma C_e-\sqrt{D}$ this implies that $-1<\lambda<0$. This completes the proof of the lemma.

The next results concern the asymptotic behaviour in the endemic case. Note that, in this case, the basic reproduction number

$$\mathcal{R}_0 = \sqrt{\frac{N}{K}} > 1.$$

This parameter is dependent on the size of population and on all parameters controlling the contamination. All this is reflected in the following proposition:

Proposition 5. If the size of the population N satisfies $K < N < \theta K$ then the infection remains endemic and the solution of the system tends to the endemic point P_e .

Proof. Suppose $K < N < \theta K$ and take into account the bound α defined in Proposition 4.

If $K < N < \alpha K$, then q + s > 1 and from Proposition 4 and Lemma 1 we have $\rho(A) < 1$ and the model is stable.

If $\alpha K < N < \theta K$, from Proposition 4, A has two positive eigenvalues and one negative eigenvalue. By Lemma 1 and Lemma 2 all eigenvalues have modulus smaller than 1. Hence, the linear system (2) is asymptotically stable to $\hat{x}_e = 0$. Then, the infection remains endemic and the solution of the system (1) tends to the point P_e .

Remark 1. If $N > \theta K$, the spectral radius of \hat{A} is greater than 1. A

Remark 2. $C(t) \leq \frac{q}{\sigma}$ is a condition to ensure that the system (1) has positive solution. Thus, if $N > \theta K$ and we compel $q - \sigma C_e \geq 0$ in P_e , then we have $(1-s)q + \sigma \beta K \ge \sigma \beta N$ which implies $N < K\left(1 + \frac{q}{1-q}\right)$. As $\theta < \left(1 + \frac{q}{1-a}\right)$, hence $\frac{2(q+s)}{q(s+1)} < 1$ and 2s + q < 1.

This occurs when the disease is devastating with the survival rate of infected individual less than the mortality rate of the pathogen. This fact is not usual in the common infectious disease, such as Salmonella, therefor it is more realistic that q + s > 1.

Remark 3. From comment in Section 1 we suppose $\frac{\beta N}{1-s} < \frac{q}{\sigma}$. That is, the size of the population N satisfies $N < \nu K$, where $\nu = \frac{q}{1-q}$. Hence, $PT = \nu K$ is a population threshold to ensure the good running of the model.

To $N<\nu K$, and attending to the value of the parameter q we have the following conclusions: if $q<\frac{1}{2}$, then N< K and from Proposition 2 the distribution of the population tends to the disease-free equilibrium point and the disease disappears; if $q>\frac{1}{2}$, then if N< K the disease disappears and if $K< N<\nu K$, the disease remains but from Proposition 5 the permanent infection tends to the endemic point.

3. Numerical results. In this section we show some numerical examples of the model 1 to illustrate our results. The main ingredient at the base of our results is to determine the number of individuals/animals which ensure the eradication of the disease or remaining endemic around the point P_e .

Consider a population which may be affected by some contagious disease transmitted through a contaminated environment. An initial infection can spread in the population living in that environment. To carry out the numerical simulations, we consider, for instance, the density of the bacteria produced by a host is $\beta = 10^2$, the survival rate of the bacteria is s = 0.9 and the exposition rate is s = 0.9. According to the values of the survival rate of the infected population s = 0.9 we consider several cases:

- The infectious disease is devastating with a survival rate q=0.4. From these data we have K=60 and the population threshold $PT=\nu K=40$. Thus, if the population is less than PT=40 we can ensure that the population tends to the disease-free equilibrium point and the condition $q-\sigma C(t)>0$ holds for all $t\geq 0$.
- Now, q = 0.9. Then K = 10 < 90 = PT. From Proposition 2 we only have a population less than K = 10 hens to ensure that the basic reproductive number $\mathcal{R}_0 = 0.1N < 0.1K = 1$, and consequently the population tends to disease-free equilibrium point. Obviously, this situation is not considered since the population is too small.

In general, the Salmonella disease does not disappear but from Propositions 2 and 5 we observe that when the population N is such that $K=10 < N < \theta K = 190$, we can ensure that the system evolves to the endemic point, keeping the disease in the henhouse but without producing a pandemic. Moreover, when the henhouse has a hen population N below the population threshold, K=10 < 0

 $N < 90 = \nu K = PT$, the disease is well controlled and we can ensure that the model considered is a good representative of the dynamic process since for all $t \ge 0$ the condition $q - \sigma C(t) > 0$ is ensured.

For example, if N=89, then $\mathcal{R}_0=8.9$ and the expected number of secondary bacteria and secondary hosts from an initial primary host increase and the solution of the system does not tend to the disease-free equilibrium point. But the matrix \hat{A} has eigenvalues less than one $\{0.91, 0.9, 0.09\}$, hence the system is asymptotically stable to the endemic equilibrium point given, in this case, by $(S_e, I_e, C_e) = (10, 79, 79, 000)$.

If we consider N=150, then the system is stable but note that the endemic equilibrium point $(S_e, I_e, C_e) = (10, 140, 140, 000)$ satisfies $q - \sigma C_e < 0$. From an initial infected individual, for time t=35 the condition $q - \sigma C(t) > 0$ is not satisfied and the last relation is not admissible.

Acknowledgments. The authors wish to express their thanks to the reviewers for helpful comments and suggestions.

REFERENCES

- [1] Cantó B., S. Cardona, C. Coll, J. Navarro-Laboulais, E. Sánchez (2012) Dynamic optimization of a gas-liquid reactor, J. Math. Chem., **50**, 381–393.
- [2] Diekmann O., M. Gyllenberg, J. Metz (2003) Steady-state analysis of structured population models, Theor. Popul. Biol., 63, 309–338.
- [3] Vanlier J., C. Tiemann, P. Hilbers, N. van Riel (2013) Parameter uncertainty in biochemical models described by ordinary differential equations, Math. Biosci., 246, 305–314.
- [4] Cantó B., C. Coll, E. Sánchez (2014) On stability and reachability of perturbed positive systems, Adv. Differ. Equ., 296, 1–1.
- [5] Cantó B., C. Coll, E. Sánchez (2013) Structured parametric epidemic model, Int. J. Comput. Math., 1–10.
- [6] Cantó B., C. Coll, E. Sánchez (2014) A study on vaccination models for a seasonal epidemic process, Appl. Math. Comput., **243**, 152–160.
- [7] Cao H., H. Zhou (2012) The discrete age-structured SEIT model with application to tuberculosis transmission in china, Math. Comput. Model., **55**, 385–395.
- [8] Hernández-Cerón N., Z. Feng Z, P. van den Driessche (2013) Reproduction numbers for discrete-time epidemic models with arbitrary stage distributions, J. Differ. Equ. Appl., 19(10), 1671–1693.
- [9] Beaumont C., J. Burie, A. Ducrot, P. Zongo (2012) Propagation of salmonella within an industrial hen house, SIAM J. Appl. Math., **72**(4), 1113–1148.

[10] Prévost K., P. Magal, J. Protais, C. Beaumont (2008) Effect of genetic resistance of the hen to salmonella carrier-state on incidence of bacterial contamination: synergy with vaccination, Vet. Res. BioMed Central. **39**(2), 1–12.

Institut de Matemàtica Multidisciplinar Universitat Politècnica de València Camino de Vera s/n, 46022, Valencia, España e-mail: bcanto@mat.upv.es mccoll@mat.upv.es esanchezj@mat.upv.es