Analysis a two strain infectious disease

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RÉSUMÉ. Un exemple typique de modèle compartimental de transmission avec traitement antibiotique et vaccination, qui peut être étudié algébriquement est présenté. Les méthodes exactes du calcul formel sont utilisées pour déterminer les quatre équilibres du système d'équations différentielles ordinaires représentant le modèle et étudier leur stabilité ainsi que leurs bifurcations.

ABSTRACT. A typical example of a compartmental desease transmission model with antibiotic treatment and vaccination that can be dealt with algebraically is presented. Methods from computer algebra are used to find the four equilibria of the ordinary differential equations characterizing the model and to study their stability as well as their bifurcations.

MOTS-CLÉS : modèle, souche, antibiotique, vaccination, équilibre, stabilité, bifurcation transcritique, taux de reproduction effectif.

KEYWORDS : model, strain, antibiotic,vaccination, equilibrium, stability, transcritical bifurcation, effective reproduction number.

1. Introduction

Compartmental models are a classical tool to model the spread of infectious diseases. Such models have the important feature of being simple enough to allow effective computation but also sufficiently flexible to take into account several behaviors of infectious diseases such as latency, the effect of treatment as well as vaccination [1]. Usually, compartmental models lead to systems of ordinary differential equations (ODE) depending on parameters having a *disease free equilibrium* E_0 characterized by the absence of disease in the population. The most fundamental question is then to find conditions on the parameters so that the disease free equilibrium is globally (or at least locally) asymptotically stable. Many compartmental models have the following behavior : the disease free equilibrium is asymptotically stable if and only if a threshold quantity depending on the parameters, called the *basic reproduction number* and denoted R_0, is < 1. When $R_0 = 1$ a new equilibrium E_1 called the *endemic equilibrium* appears and exchanges stability with the disease free equilibrium through a transcritical bifurcation so that, when $R_0 > 1$, the equilibrium E_1 is asymptotically stable while E_0 is unstable. Such a behavior no longer holds when for example the pathogen agent responsible of the disease transmission has several strains.

In this paper we introduce and study a compartmental model of an infectious disease caused by a two-strain bacterial pathogen. We show how to use methods from real algebraic geometry [6] and computer algebra [5] to find all the equilibria of the ODE system describing the model and to study their stability as well as their bifurcations.

The paper is structured as follows. In Section 2 we present the details of the model. In Section 3 we compute the equilibria of the model by using Groebner bases theory [5]. The stability of these equilibria is then studied in Section 4. A relation between our study and the effective reproduction number is given in Appendix A. We also give details on the bifurcations of the equilibria in Appendix C and a simulation of the vaccination effect in Appendix D.

2. Presentation of the model

The model concerns a host population, a part of its individuals are under antibiotic (Ab) treatment against a two-strain bacterial pathogen. Individuals who are not under Ab treatment can be colonized by an antibiotic-susceptible (Ab-S) strain or by an antibiotic-resistant (Ab-R) strain of a bacterial pathogen, but not by both at the same time (i.e., there is a maximal competition between the two strains), while those under antibiotic treatment can only be colonized by the Ab-R strain. We assume there is a fitness cost for resistance such that the Ab-R strain is somewhat less transmissible than the Ab-S strain.

The host population is divided into seven compartments representing the fractions of the population in each state. There are four states representing individuals not under Ab treatment, namely susceptible individuals (S), colonized individuals by the Ab-S strain (I_1), colonized individuals by the Ab-R strain (I_2) and vaccinated individuals (V). The individuals in V are assumed to have a temporary complete immunity to infection by both strains. There are three states for individuals under Ab treatment, namely susceptible individuals (T), colonized individuals by the Ab-R strain (T_2) and vaccinated individuals who are currently under Ab treatment (V_T). As well as individuals in V, those in V_T are

assumed to have a temporary complete immunity against infection by both strains. The transfer diagram of the model is given in the following figure.

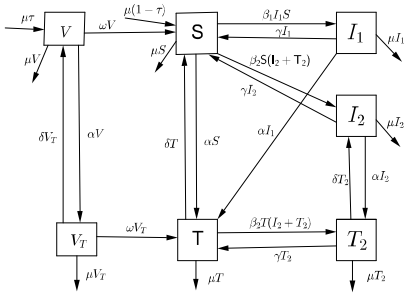


Figure 1. *Transfer diagram*

Mathematically, the model is represented by a parameter-dependent ODE system (E) of the form $\dot{x} = f(x, u)$, where the components of f are polynomials in terms of the states variables $x = (S, I_1, T, T_2, I_2, V, V_T)$ and the parameters $u = (\alpha, \beta_1, \beta_2, \gamma, \delta, \mu, \tau, \omega)$ as well. More precisely, the ODE system writes as

$$\begin{aligned}
\dot{S} &= \mu(1-\tau) + \omega V - \alpha S - \beta_1 S I_1 + \gamma I_1 + \delta T - \mu S - \beta_2 S I_2 - \beta_2 S T_2 + \gamma I_2 \\
\dot{I}_1 &= \beta_1 I_1 S - \gamma I_1 - \alpha I_1 - \mu I_1 \\
\dot{T} &= \omega V_T + \alpha S - \delta T - \beta_2 T I_2 - \beta_2 T T_2 + \gamma T_2 + \alpha I_1 - \mu T \\
\dot{T}_2 &= \beta_2 T I_2 + \beta_2 T T_2 - \gamma T_2 + \alpha I_2 - \delta T_2 - \mu T_2 \\
\dot{I}_2 &= \beta_2 S I_2 + \beta_2 S T_2 - \gamma I_2 - \alpha I_2 + \delta T_2 - \mu I_2 \\
\dot{V} &= \mu\tau + \delta V_T - (\alpha + \mu + \omega) V \\
\dot{V}_T &= \alpha V - (\mu + \omega + \delta) V_T
\end{aligned}$$

where
α is the Ab treatment rate,
δ is the rate at which the effect of Ab treatment ends,
β_1 is the Ab-S strain transmission rate,
β_2 is the Ab-R strain transmission rate,
γ is the clearance rate,
μ is the birth rate which is assumed to be equal to the mortality rate,
τ is the vaccination coverage,
ω is the waning rate of vaccine efficiency.

The time scale here is the year and rates are expressed in terms of $1/t$. For example, $\alpha = 0.5$ means that an antibiotic treatment takes place every 2 years in average for each individual. The parameters $(\alpha, \gamma, \delta, \tau, \omega)$ are nonnegative while β_1, β_2, μ are positive.

One readily checks that $\mathbb{R}^7_+$ est positively invariant under the action of the vector field $f(x, u)$. On the other hand, if we let $P = S + I_1 + T + T_2 + I_2 + V + V_T$ then by summing up the seven equations in (E) we obtain

$$P' = \mu(1 - P)$$

and hence the affine hyperplane $P = 1$ is invariant under the action of the vector field $f(x, u)$. Thus, the set

$$\Omega = \{(S, I_1, T, T_2, I_2, V, V_T) \in \mathbb{R}^7_+ \mid S + I_1 + T + T_2 + I_2 + V + V_T = 1\}$$

is positively invariant under the action of $f(x, u)$. As we assume the host population to be constant we only need to study the dynamics of the ODE system (E) in the compact Ω.

3. Equilibria of the model

As we already have mentioned, the right hand side of the every equation in (E) is a polynomial in terms of the state variables and the parameters. Therefore, to find the equilibria of (E) we can resort to Groebner bases theory, e.g. ; [5]. Notice that we are only interested in equilibria whose components are nonnegative and sum up to 1. Thus, to obtain the equilibria of the model we need first to solve the system of polynomial equations formed by the equation $S + I_1 + T + T_2 + I_2 + V + V_T = 1$ together with the seven equations obtained from (E) by putting to 0 the left hand side. The two last equations obtained from (E) form in fact a linear system whose unique solution is

$$(v, v_T) = \left(\frac{\mu\,\tau\,(\delta + \mu + \omega)}{(\mu + \omega)\,(\alpha + \delta + \mu + \omega)}, \frac{\mu\,\tau\alpha}{(\mu + \omega)\,(\alpha + \delta + \mu + \omega)} \right).$$

These will be the two last components of every equilibrium of the model. After respectively substituting v and v_T to V and V_T and then computing a Groebner basis of the obtained system with respect to the lexicographic order $S \prec I_1 \prec T \prec T_2 \prec I_2$ we obtain an equivalent, and much simpler, system (G) consisting of 6 equations. The first one depends only on S and has degree 3. Moreover, its three roots are all nonnegative and are given as

$$\begin{aligned} s_0 &= \frac{S_0}{D_0} \\ s_1 &= \frac{c}{\beta_1} \\ s_2 &= \frac{S_2}{D_2} \end{aligned}$$

with

$$\begin{aligned} c &= \alpha + \gamma + \mu \\ S_0 &= \mu(\alpha + \delta + \mu)(\delta + \mu + \omega)(1 - \tau) + \omega(\alpha\delta + (\delta + \mu)(\delta + \mu + \omega)) \\ D_0 &= (\mu + \omega)\,(\alpha + \delta + \mu)\,(\alpha + \delta + \mu + \omega) \\ S_2 &= \delta(\gamma + \mu)D_0 + (S_{21} + \omega(S_{22}(1 - \tau) + S_{23}) + \omega^2 S_{24})\beta_2 \\ D_2 &= (\alpha + \delta + \mu)(\alpha + \delta + \mu + \omega)\,(\beta_2(\mu(1 - \tau) + \omega) + (\delta + \alpha)(\mu + \omega))\,\beta_2, \end{aligned}$$

where

$$\begin{aligned} S_{21} &= \mu(\alpha + \delta + \mu)(1 - \tau)(\gamma\delta + \mu(\alpha + \gamma + \delta + \mu)) \\ S_{22} &= \mu c(\alpha + \delta + \mu) \\ S_{23} &= (\delta + \mu)^2(\gamma + \mu) + \alpha(\gamma\delta + \mu(\delta + \mu)) \\ S_{24} &= \gamma\delta + \mu(\alpha + \gamma + \delta + \mu) \end{aligned}$$

are positive quantities.

After specializing the variable S to s_0 in the system (G) and then solving for the other variables we obtain a unique solution E_0, whose coordinates are

$$\left(s_0, 0, \frac{T_0}{D_0}, 0, 0, v, v_T\right)$$

with

$$T_0 = \alpha(\mu(\alpha+\delta+\mu)(1-\tau)+\omega(\alpha+\delta+2\mu+\omega).$$

This is the disease free equilibrium of the model. Clearly, its coordinates are non-negative and so it has an epidemiological meaning for all the values of the parameters. Moreover the sum of its coordinates is equal to 1.

By substituting s_2 to S in the system (G) and then solving for the other variables we obtain a unique solution

$$E_2 = \left(s_2, 0, \frac{T_2}{D_2}, \frac{A_2 T_{22}}{D_2(\mu+\omega)}, \frac{A_2 I_{22}}{D_2(\mu+\omega)}, v, v_T\right)$$

where

$$\begin{array}{rcl} A_2 & = & (\mu(1-\tau)+\omega)\beta_2 - (\gamma+\mu)(\mu+\omega) \\ T_2 & = & T_{21}\beta_2 + (\gamma+\mu)D_0 \\ T_{22} & = & \mu(\alpha+\delta+\mu)(1-\tau)+\omega(\alpha+\delta+2\mu+\omega)\beta_2 + D_0 \\ I_{22} & = & I_{221}\beta_2 + I_{222} \end{array}$$

where

$$\begin{array}{rcl} T_{21} & = & \gamma\mu(\alpha+\delta+\mu(1-\tau)+\omega(\gamma(\alpha+\delta+2\mu+\omega)+\mu(\alpha+\delta+\mu)\tau) \\ I_{221} & = & \mu(\alpha+\delta+\mu)(\delta+\mu+\omega)(1-\tau)+\omega(\alpha\delta+(\delta+\mu+\omega)(\delta+\mu)) \\ I_{222} & = & \delta((\alpha+\delta+\mu)\omega(\alpha+\delta 2\mu+\omega)+\mu((\delta+\mu)^2+\alpha(\alpha+2\delta+2\mu))) \end{array}$$

Clearly, $T_2 \geq 0$, $I_{22} \geq 0$ et $I_{22} \geq 0$. Thus, E_2 has an epidemiological meaning if and only if $A_2 \geq 0$. Moreover the sum of its coordinates is equal to 1. This equilibrium, when its exists, corresponds to the absence of the first strain of the bacterial pathogen.

For $S = s_1$, and when solving (G) for the other variables, we obtain two equilibria E_1 and E_3. The coordinates of E_1 are

$$\left(s_1, \frac{A_1}{D_0\beta_1}, \frac{T_0}{D_0}, 0, 0, v, v_T\right)$$

with

$$A_1 = S_0\beta_1 - cD_0$$

This equilibrium has an epidemiological meaning if and only if $A_1 \geq 0$. Moreover the sum of its coordinates is equal to 1.

The coordinates of E_3 are

$$\left(s_1, \frac{A_3}{cD_0\beta_2(\beta_1-\beta_2)}, \frac{T_3}{\beta_1\beta_2}, \frac{A_4}{D_0\beta_1\beta_2}, \frac{A_4 I_3}{cD_0\beta_1\beta_2(\beta_1-\beta_2)}, v, v_T\right)$$

where

$$\begin{array}{rcl} A_3 & = & \delta(\gamma+\mu)D_0\beta_1 + A_{31}\beta_2 + (A_{32}(1-\tau)+\omega(A_{33}\omega+A_{34})\beta_1\beta_2 \\ T_3 & = & (\gamma+\mu)\beta_1 - c\beta_2 \\ A_4 & = & -(\gamma+\mu)D_0\beta_1 + cD_0\beta_2 + A_{41}\beta_1\beta_2 \\ I_3 & = & \delta\beta_1 + c\beta_2 \end{array}$$

with

$$\begin{aligned}
A_{31} &= -c(\alpha+\delta+\mu)(\alpha+\delta+\mu+\omega)(((1-\tau)\mu+\omega)\beta_2+(\alpha+\delta)(\mu+\omega)) \\
A_{32} &= \mu(\alpha+\delta+\mu)(\delta(\gamma-\omega)+(\mu+\omega)(\alpha+\gamma+\delta+\mu)) \\
A_{33} &= \gamma\delta+\mu(\alpha+\gamma+\delta+\mu) \\
A_{34} &= (\delta+\mu)^2(\gamma+\mu)+\alpha(\delta(\gamma+\mu)+\mu^2) \\
A_{41} &= \alpha((\alpha+\delta+2\mu)\omega+\mu(\alpha+\delta+\mu)(1-\tau)+\omega^2)
\end{aligned}$$

The coordinates of E_3 are nonnegative if and only if $A_3 \geq 0$, $T_3 \geq 0$ and $A_4 \geq 0$. The fact that $T_3 \geq 0$ follows from the fact that $A_3 \geq 0$ (details are given in Appendix B). Moreover the sum of its coordinates is equal to 1. Thus, E_3 has an epidemiological meaning if and only if $A_3 \geq 0$ and $A_4 \geq 0$.

4. Stability of equilibria

In this section we study the local asymptotic stability of the four equilibria of the model. To this aim, we use the classical technique which consists in linearizing the system around the given equilibrium.

In the rest of this paper we let

$$Q_0 = (Z+\mu)(Z+\mu+\omega)(Z+\alpha+\delta+\mu)(Z+\alpha+\delta+\mu+\omega).$$

This polynomial is a common factor of the characteristic polynomials of all the four equilibria.

The characteristic polynomial P_0 of the Jacobian matrix $\partial_x f(u, E_0)$ factorizes as follows [7].

$$P_0 = (Z+c')\left(Z-\frac{A_1}{D_0}\right)\left(Z-\frac{A_2}{\mu+\omega}\right)Q_0,$$

with $c' = \alpha+\gamma+\delta+\mu$ Hence, the equilibrium E_0 is hyperbolic and locally asymptotically stable if and only if $A_1 < 0$ and $A_2 < 0$.

Concerning the equilibrium E_1, we have the following factorization of the characteristic polynomial P_1 of the Jacobian matrix $\partial_x f(u, E_1)$.

$$P_1 = (Z+c')\left(Z+\frac{A_1}{D_0}\right)\left(Z-\frac{A_4}{D_0\beta_1}\right)Q_0.$$

This shows that E_1 is hyperbolic and locally asymptotically stable if and only if $A_1 > 0$ and $A_4 < 0$.

For the equilibrium E_2, the characteristic polynomial P_2 of the Jacobian matrix $\partial_x f(u, E_2)$ factorizes as follows.

$$P_2 = (Z+c')\left(Z+\frac{A_2}{D_0}\right)\left(Z-\frac{A_3}{D_0\beta_1}\right)Q_0.$$

This shows that E_2 is hyperbolic and locally asymptotically stable if and only if $A_2 > 0$ and $A_3 < 0$.

The characteristic polynomial P_3 of the Jacobian matrix $\partial_x f(u, E_3)$ at the equilibrium E_3 does not completely factorize. We have in fact

$$P_3 = (Z^3+q_2Z^2+q_1Z+q_0)Q_0,$$

where q_0, q_1, q_2 are polynomials in terms of the parameters. We apply for this case the classical Liénard-Chipart criterion, e.g. ; [6], to the polynomial $Z^3 + q_2 Z^2 + q_1 Z + q_0$.

When we respectively substitute s_3 and t_3 to S and T we obtain

$$\begin{array}{rcl} q_0 & = & c\, I_1\, (I_2 + T_2)\, \beta_2\, (\beta_1 - \beta_2) \\ q_1 & = & (c' + (T_2 + I_2)\beta_2)\, ((T_2 + I_2)\beta_2 + I_1\beta_1) \\ q_2 & = & c + 2\, (I_2 + T_2)\, \beta_2 + I_1\, \beta_1 \end{array}$$

All three quantities are positive provided that E_3 has positive coordinates, that is $A_3 > 0, A_4 > 0$. The quantity that remains to check is $q_0(q_2 q_1 - q_0)$. After simplification we obtain $q_2 q_1 - q_0$ equal to

$$\begin{array}{l} 2(T_2 + I_2)^3 {\beta_2}^3 + (3(T_2 + I_2)^2 I_1\beta_1 + (T_2 + I_2)(cI_1 + 3c'(T_2 + I_2)))\,{\beta_2}^2 \\ +({I_1}^2(T_2 + I_2){\beta_1}^2 + (3c' + \delta)I_1(T_2 + I_2)\beta_1 + {c'}^2(T_2 + I_2))\beta_2 \\ +c' I_1(I_1\beta_1 + c')\beta_1 \end{array}$$

which is positive at E_3 if $A_3 > 0, A_4 > 0$. Thus q_2, q_1, q_0 and $q_0(q_2 q_1 - q_0)$ are all positive at E_3 if $A_3 > 0, A_4 > 0$. The equilibrium E_3 is therefore hyperbolic and locally asymptotically stable if and only if $A_3 > 0$ and $A_4 > 0$.

We have thus the following result.

Theorem 1 *The model represented by the system (E) has four equilibria.*

1) A disease free equilibrium E_0 which exists for all values of the parameters. It is hyperbolic and locally asymptotically stable if and only if $A_1 < 0$ et $A_2 < 0$.

2) An equilibrium E_1 which exists if and only if $A_1 > 0$ and is hyperbolic and locally esymptotically stable if and only if $A_1 > 0$ and $A_4 < 0$.

3) An equilibrium E_2 which exists if and only if $A_2 \geq 0$ and is hyperbolic and locally asymptotically stable if and only if $A_2 > 0$ and $A_3 < 0$.

4) An equilibrium E_3 which exists if and only if $A_3 \geq 0$ and $A_4 \geq 0$, and is hyperbolic and locally asymptotically stable if and only if $A_3 > 0$ and $A_4 > 0$.

All the local codimension-one bifurcations of the system (E) are transcritical (details are given in Appendix C). To illustrate the results, we represent the curves $A_1 = 0$, $A_2 = 0$, $A_3 = 0$ et $A_4 = 0$ $\mathbb{R}_+ \times \mathbb{R}_+$ in termes of the parameters $0 < \beta_2 < \beta_1$. The other parameters $(\alpha, \gamma, \delta, \mu, \tau, \omega)$ are given fixed values.

The figure corresponds to $\alpha = 0.4, \gamma = 0.6, \delta = 0.3, \mu = 0.2, \tau = 0.35, \omega = 0.19$. These values have been chosen to make visible the stability domains. More realistic values, from the epidemiological point of view, could be $\alpha = 0.4, \gamma = 15, \delta = 60, \mu = 0.0125, \tau = 0.70, \omega = 0.19$.

Conclusion

In this paper we studied a two-strain compartmental model with vaccination and antibiotic treatment. All the equilibria and codimension-one local bifurcations of the model have been exactly characterized using computer algebra.

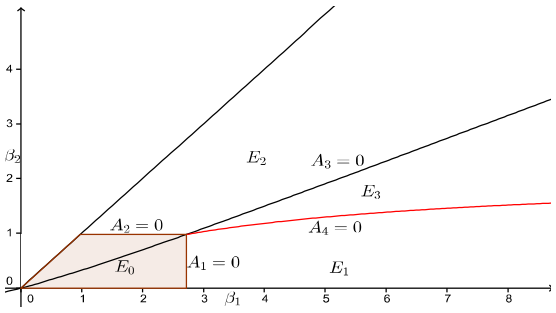


Figure 2. *Equilibria in the β_1, β_2 plane*

5. Bibliographie

[1] H. W HETHCOTE. « The mathematic of infectiouse disease. », *SIAM Rev.* , vol. 42, n° 4 : 599-653 (electronic), 2000.

[2] S. WIGGINS. « Introduction to applied nonlinear dynamical systemsand chaos », *Texts in Applied Mathematics. Springer-Verlag*, vol. 2, n° 2, 2003.

[3] N. FERGUSON, R. ANDERSON, S. GUPTA. « The effect of antibody-dependant enhancement on the transmissiondynamics and persistence of multiple strain pathogens. », *Proc. Natl. Acad. Sci. USA*, vol. 96, n° , 1999.

[4] L. BILLINGS , A. FIORILLO , I. B. SCHWARTZ. « Vaccinations in disease models with antibody-dependent enhancement. », *Math. Biosci., 2008.*, vol. 211, n° 2, 2008.

[5] D. COX , J. LITTLE., D. O'SHEA. « Ideals, varieties, and algorithms. », *Undergraduate Texts in Mathematics. Springer, New York*, vol. , n° 2, 2007.

[6] S. BASU, R. POLLACK , M.-F. ROY. « Algorithms in real algebraic geometry », *Algorithms and Computation in Mathematics. Springer-Verlag, Berlin*, vol. 10 , n° 2 , 2006.

[7] C. W. BROWN , M. EL KAHOUI , D. NOVOTNI, , A. WEBER.« Algorithmic methods for investigating equilibria in epidemic modeling. », *J. Symbolic Comput.*,vol. 41 , n° 11, 2006.

[8] P VAN DEN. DRIESSCHE , J. WATMOUGH. « Reproduction numbers and sub-threshold endemic equilibria for compartmental models of disease transmission. », *Math. Biosci*,vol. 180 , 2002.

A. Relation to the effective reproduction number

We check the results of Section 4 on the stability of the disease free equilibrium by using the notion of effective reproduction number (see [8]).

It is easy to see that the effective reproduction number of the first strain in the absence of the second one, i.e. ; $\beta_2 = 0, \beta_1 > 0$, is

$$R_{\text{eff}1} = \frac{s_0 \beta_1}{c}.$$

Also, one easily checks that the effective reproduction number of the second strain in the absence of the first one, i.e. ; $\beta_1 = 0, \beta_2 > 0$, is

$$R_{\text{eff}2} = \frac{(\mu(1-\tau)+\omega)\beta_2}{(\gamma+\mu)(\mu+\omega)}.$$

From the variations of the infectious compartments, namely

$$\begin{array}{rcl} \dot{I_1} & = & I_1 S\beta_1 - (\alpha+\gamma+\mu)I_1 \\ \dot{T_2} & = & T(I_2+T_2)\beta_2 - ((\delta+\gamma+\mu)T_2 - \alpha I_2) \\ \dot{I_2} & = & S(I_2+T_2)\beta_2 - (cI_2 - \delta T_2) \end{array}$$

and by letting $w = (I_1, T_2, I_2)$ we define

$$\mathcal{F}(w) = \begin{pmatrix} I_1 S\beta_1 \\ T(I_2+T_2)\beta_2 \\ S(I_2+T_2)\beta_2 \end{pmatrix}$$

This vector captures the rates at which new infected individuals, per infectious compartment, appear. We also define

$$\mathcal{V}(w) = \begin{pmatrix} cI_1 \\ (\gamma+\delta+\mu)T_2 - \alpha I_2 \\ cI_2 - \delta T_2 \end{pmatrix}$$

the vector whose components are the differences between the rate of individuals leaving an infectious compartment and the rate of those arriving at the same compartment. We then compute the matrices

$$F = \partial_w \mathcal{F}(w) = \begin{pmatrix} s_0\beta_1 & 0 & 0 \\ 0 & t_0\beta_2 & t_0\beta_2 \\ 0 & s_0\beta_2 & s_0\beta_2 \end{pmatrix}$$

and

$$V = \partial_w \mathcal{V}(w) = \begin{pmatrix} c & 0 & 0 \\ 0 & \gamma+\delta+\mu & -\alpha \\ 0 & -\delta & c \end{pmatrix}.$$

The matrix $F \cdot V^{-1}$ is called *the next generation matrix*, and its spectral radius is the effective reproduction number of the model.

$$F \cdot V^{-1} = \begin{pmatrix} \dfrac{s_0\beta_1}{c} & 0 & 0 \\ 0 & \dfrac{t_0\beta_2}{\gamma+\mu} & \dfrac{t_0\beta_2}{\gamma+\mu} \\ 0 & \dfrac{s_0\beta_2}{\gamma+\mu} & \dfrac{s_0\beta_2}{\gamma+\mu} \end{pmatrix}.$$

Clearly, $R_{\text{eff}1}$ is an eigenvalue of $F \cdot V^{-1}$. On the other hand, the determinant $|F \cdot V^{-1}|$ is zero, and hence 0 is an eigenvalue of $F \cdot V^{-1}$. The third eigenvalue of $F \cdot V^{-1}$ is the trace of the second block of $F \cdot V^{-1}$ and it is equal to

$$\frac{(s_0+t_0)\beta_2}{\gamma+\mu} = \frac{(\mu(1-\tau)+\omega)\beta_2}{(\gamma+\mu)(\mu+\omega)} = R_{\text{eff}2}.$$

Thus, the effective reproduction number of the model in question is $R_{\text{eff}} = \max(R_{\text{eff}1}, R_{\text{eff}2})$. This shows that E_0 hyperbolic and locally asymptotically stable if and only if $R_{\text{eff}} < 1$ [8]. This is clearly equivalent to the condition $A_1 < 0$ et $A_2 < 0$.

B. Conditions of the existence of the equilibrium E_3

As we have seen in Section 3, the equilibrium E_3 has nonnegative coordinates if and only if $A_3, T_3, A_4 \geq 0$. Here we show that $A_3 \geq 0$ implies $T_3 \geq 0$, and so E_3 has an epidemiological meaning if and only if $A_3 \geq 0$ and $A_4 \geq 0$. Let

$$\begin{aligned} D &= \mu\,(\alpha+\delta+\mu)\,(1-\tau)\;((\mu+\omega)c+\delta(\gamma+\mu))\,\beta_2+R, \\ R &= \omega(\alpha\delta\gamma+(\delta+\mu)(\delta+\mu+\omega)+\mu(\alpha+\delta+\mu)(\delta+\mu+\omega))\beta_2+\delta(\gamma+\mu)D_0, \end{aligned}$$

Then we have

$$T_3 = \frac{\gamma+\mu}{D}A_3 + \frac{N}{D}$$

with

$$\begin{aligned} N &= \gamma\mu(\alpha+\delta+\mu)((1-\tau)\beta_2+(\alpha+\delta+\mu)(\gamma+\mu))+\omega L+\omega^2 M \\ M &= \mu c'+\gamma(\alpha+\delta+\beta_2) \\ L &= (\gamma+\mu)\alpha^2+((2\delta+3\mu)(\gamma+\mu)+\alpha(\gamma+\mu\tau)\beta_2)+K \\ K &= (\gamma+\mu)\delta^2+\delta(3\mu(\gamma+\mu)+(\gamma+\mu\tau)\beta_2)+\mu(2\mu^2+2\mu\gamma+2(\gamma+\mu\tau)\beta_2) \end{aligned}$$

which shows that $T_3 \geq 0$ whenever $A_3 \geq 0$.

C. Codimension-one bifurcations of equilibria

In this section we study the local codimension-one bifurcations of the system (E) when the parameters change. It turns out that all such bifurcations have a transcritical nature.

Stability exchange between E_0 and E_1. As we have seen, the equilibrium E_0 is hyperbolic and locally asymptotically stable if and only if $A_1 < 0$ and $A_2 < 0$. Moreover, E_1 has an epidemiological meaning if and only if $A_1 \geq 0$. When $A_1 = 0$, E_0 and E_1 become the same and their common characteristic polynomial

$$P_{01} = Z(Z+c')\left(Z - \frac{A_2}{\mu+\omega}\right)Q_0$$

has 0 as a simple root, while the other ones are negative. Thus, when A_1 moves from negative values to positive ones, E_0 becomes unstable while E_1 gains stability as long as $A_2 < 0$.

Stability exchange between E_0 and E_2. When $A_2 = 0$ and $A_1 < 0$ the two equilibria E_0 and E_2 become the same and their common characteristic polynomial

$$P_{02} = Z(Z+c')\left(Z - \frac{A_1}{D_0}\right)Q_0$$

has 0 as a simple root, while the others are negative. When A_2 moves from negative values to positive ones the equilibrium E_0 becomes unstable, while E_2 gains stability as long as $A_1 < 0$.

Stability exchange between E_2 and E_3. When $A_3 = 0$ and $A_2 > 0$ the two equilibria E_2 and E_3 are the same and their common characteristic polynomial

$$P_{23} = Z\left(Z + \frac{(\mu(1-\tau)+\omega)\beta_2 + (\alpha+\delta)(\mu+\omega)}{\mu+\omega}\right)\left(Z + \frac{A_2}{\mu+\omega}\right)Q_0$$

has 0 as simple root while the other ones are negative. Thus, when A_3 moves from negative values to positive ones the equilibrium E_2 becomes unstable while E_3 gains stability as long as $A_2 > 0$.

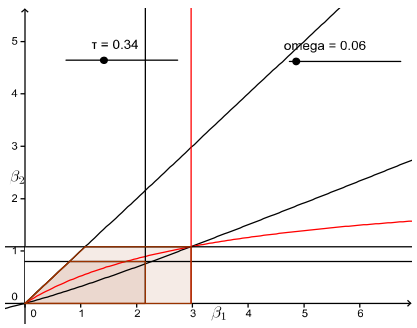
Stability exchange between E_1 and E_3. When $A_4 = 0$ and $A_1 > 0$ the two equilibria E_1 and E_3 become the same and their common characteristic polynomial

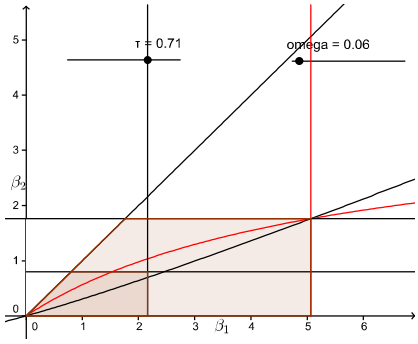
$$P_{13} = Z(Z + c')\left(Z + \frac{A_1}{D_0}\right)Q_0$$

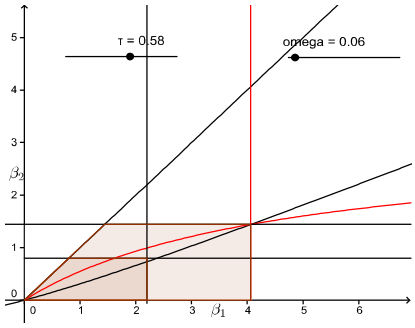
has 0 as simple root while the other are negative. Thus, when A_4 moves from negative values to positive ones E_1 becomes unstable while E_3 becomes stable as long as $A_1 > 0$

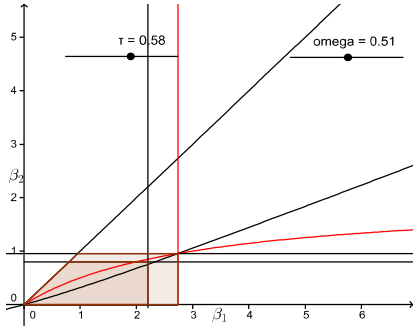
D. Simulation of the vaccination effect

In this section the parameters μ, γ, α and δ are given fixed values. For several values of τ and ω (the vaccination parameters) we represent the curves $A_1 = 0$, $A_2 = 0$, $A_3 = 0$ and $A_4 = 0$ as functions of $(\beta_1, \beta_2) \in \mathbb{R}^2_+$. The light-colored regions represent the domain of stability of the disease free equilibrium in the presence of vaccination, while the dark-colored ones correspond to the absence of vaccination. The figures show that the stability domain of E_0 increases in terms of τ but decreases in terms of ω.




τ = 0.71
omega = 0.06
β_2
β_1


τ = 0.58
omega = 0.06
β_2
β_1


τ = 0.58
omega = 0.51
β_2
β_1