The SEIRS epidemic model (an example of qualitative analysis)

The classic SEIRS model is given by the system of ODEs

\[
\begin{align*}
S'(t) &= \mu N + cR - \beta SI/N - \mu S, \\
E'(t) &= \beta SI/N - (\mu + k)E, \\
I'(t) &= kE - (\mu + \gamma)I, \\
R'(t) &= \gamma I - (\mu + c)R,
\end{align*}
\]

with the total population \( N = S + E + I + R \). (We assume a large established population, so that we can use standard incidence \((\beta SI/N)\) and assume \(N\) constant over time.) \( S \) is the susceptible class, \( E \) the exposed (latent) class, \( I \) the infectious class, and \( R \) the temporarily immune class.

If we look for equilibria, we find two: the disease-free equilibrium (DFE), \((S^*, E^*, I^*, R^*) = (N, 0, 0, 0)\), and the endemic equilibrium (EE), which has

\[
\frac{S^*}{N} = \frac{1}{R_0}, \quad \text{where} \quad R_0 = \frac{\beta k}{\mu + \gamma} \frac{1}{\mu + k}
\]

gives the infection’s basic reproductive number. (Note it is independent of \(c\).) We can then calculate the remaining components of the EE:

\[
\begin{align*}
\frac{E^*}{N} &= \frac{(\mu + \gamma)(\mu + c)}{(\mu + \gamma + k)(\mu + c) + k\gamma} \left( 1 - \frac{1}{R_0} \right), \\
\frac{I^*}{N} &= \frac{k(\mu + c)}{(\mu + \gamma + k)(\mu + c) + k\gamma} \left( 1 - \frac{1}{R_0} \right), \\
\frac{R^*}{N} &= \frac{k\gamma}{(\mu + \gamma + k)(\mu + c) + k\gamma} \left( 1 - \frac{1}{R_0} \right),
\end{align*}
\]

which leaves us with only one problem: these last three components might be negative, which would make the equilibrium biologically meaningless. The EE is biologically meaningful if and only if \((\text{iff})\) \(R_0 > 1\). Otherwise only one equilibrium (the DFE) exists within our nonnegative state space.

The next step in qualitative analysis of a dynamical system is a local stability analysis for each equilibrium. For that, we calculate the system’s Jacobian matrix,

\[
J = \begin{bmatrix}
-(\mu + \beta I^*/N) & 0 & -\beta S^*/N & c \\
\beta I^*/N & -(\mu + k) & \beta S^*/N & 0 \\
0 & k & -\mu + \gamma & 0 \\
0 & 0 & \gamma & -(\mu + c)
\end{bmatrix}.
\]

Substituting \((S^*, E^*, I^*, R^*) = (N, 0, 0, 0)\), we find

\[
J(DFE) = \begin{bmatrix}
-\mu & 0 & -\beta & c \\
0 & -(\mu + k) & \beta & 0 \\
0 & k & -(\mu + \gamma) & 0 \\
0 & 0 & \gamma & -(\mu + c)
\end{bmatrix}.
\]

By inspection we see the first eigenvalue is \(-\mu < 0\) (since all the entries below it are 0); this lets us eliminate the first row and column. Now the last eigenvalue is seen to be \(-(\mu + c) < 0\), since all the remaining entries above it are 0; this lets us eliminate the last row and column, leaving us with the interior \(2 \times 2\) submatrix \(A\), to which we apply the \((2-D)\) Routh-Hurwitz criteria, trace \(A < 0\) and
The Jacobian at the EE does not simplify so neatly, which leaves us with the Routh-Hurwitz criteria for 4-D systems to apply. Since this is likely to be rather painful, we will instead employ a trick to simplify the eventual calculation: We will reduce the dimension of the system by eliminating the $S$ variable and differential equation, rewriting it in $dE/dt$ as $S = N - E - I - R$. This yields a 3-D system, with a 3-D Jacobian matrix at the EE

$$J_3 = \begin{bmatrix} -(\mu + k + \beta I^*/N) & \beta(S^* - I^*)/N & -\beta I^*/N \\ k & -(\mu + \gamma) & 0 \\ 0 & \gamma & -(\mu + c) \end{bmatrix}.$$

Now we write the characteristic equation $\det(J_3 - \lambda I_3) = 0$ (where $I_3$ is the $3 \times 3$ identity matrix) in the form

$$\lambda^3 + a_1 \lambda^2 + a_2 \lambda + a_3 = 0,$$

in order to apply the Routh-Hurwitz criteria for a 3-D system: (i) $a_1 > 0$, (ii) $a_3 > 0$, (iii) $a_1 a_2 > a_3$. It is simplest to use a computer algebra system such as Mathematica to verify symbolically that the three criteria hold when $R_0 > 1$:

$$a_1 = c + \gamma + \beta I^*/N + k + 3\mu,$$

$$a_3 = (\mu + c)(\mu + k)(\mu + \gamma)(R_0 - 1),$$

$$a_1 a_2 - a_3 = (c + \mu)\left\{c(\gamma + k + \mu)\left[\gamma^2 + \beta k + (k + \mu)^2 + \gamma(k + 2\mu)\right] + \gamma^2(4k^2 + 7\mu) + \gamma^2(2\beta k + 6k^2 + 19k\mu + 15\mu^2) + \beta^2 k^2 + (k + \mu)^3(k + 4\mu) + \gamma k^3 + 19k^2 \mu + 28k\mu^2 + \beta k(3k + 7\mu) + 13\mu^3 + \beta k(2k^2 + 7k\mu + 5\mu^2)\right\} + c^2 k^2(\gamma + k + 3\mu) + (\gamma + \mu)(k + \mu)\left[\gamma^3 + \gamma^2(4k + 6\mu) + \gamma(2k + 3\mu)^2 + (k + \mu)^2(k + 4\mu)\right] + \beta k(\gamma^3 + k^3 + 6k^2\mu + 12k\mu^2 + 7\mu^3 + 2\gamma(2k + 3\mu) + \gamma(2k^2 + 11k\mu + 12\mu^2)) + (\gamma + \mu)^3(k + \mu)^2 + \beta^2 k^2(\gamma + k + 2\mu) + \beta k(\gamma + \mu)(k + \mu)(\gamma^2 + k^2 + 3k\mu + 3\mu^2 + \gamma(k + 3\mu))\} / [(\mu + \gamma)(\mu + k) + c(\mu + \gamma + k)]^2$$

After all that, it seems somehow unfair that we are not yet finished, but all this has only proven local asymptotic stability for each equilibrium. We must now consider global asymptotic stability, and the telescoping structure of the original system gives us an excellent opportunity to try a Lyapunov function. In particular, in order to make terms telescope, we try $V = E + \frac{\mu + k}{k} I$. This is a Lyapunov-like function for the DFE since $V$ is only positive semidefinite away from the DFE ($V = 0$ if $E = I = 0$), and $dV/dt$ is negative semidefinite if $R_0 < 1$:

$$dV/dt = dE/dt + \frac{\mu + k}{k} dI/dt = \beta SI/N - (\mu + \gamma)\frac{\mu + k}{k} I \leq \beta \left(1 - \frac{1}{R_0}\right) I.$$

In order to prove the DFE is GAS, we need the following result:

**LaSalle’s Invariance Principle**: Given a weak Lyapunov function $V(x)$ for a system $dx/dt = f(x)$ with equilibrium $x^*$ (i.e., $V$ is $C^1$ and positive definite on the domain of $f$, and $dV/dt$ is negative semidefinite on the domain of $f$, with $V(x^*) = dV/dt(x^*) = 0$), then $x^*$ is GAS if $x^*$ is the only invariant subset of the set $\{x : dV/dt(x) = 0\}$. (More generally, the largest invariant subset of this set is globally attracting.)

The largest invariant subset of $\{(E, I, R) : I = 0\}$ is $\{(E, I, R) : E = I = 0\}$, so the latter set is globally attracting. But on this set $dR/dt < 0$ so $(E, I, R) \to (0, 0, 0)$; hence the DFE is GAS. Global stability of the EE for the SEIRS model has long been conjectured but never proven!