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EPIDEMIC THRESHOLD CONDITIONS FOR SEASONALLY FORCED SEIR MODELS

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Abstract. In this paper we derive threshold conditions for eradication of diseases that can be described by seasonally forced susceptible-exposed-infectious-recovered (SEIR) models or their variants. For autonomous models, the basic reproduction number $\mathcal{R}_0 < 1$ is usually both necessary and sufficient for the extinction of diseases. For seasonally forced models, $\mathcal{R}_0$ is a function of time t. We find that for models without recruitment of susceptible individuals (via births or loss of immunity), $\max_t\{\mathcal{R}_0(t)\} < 1$ is required to prevent outbreaks no matter when and how the disease is introduced. For models with recruitment, if the latent period can be neglected, the disease goes extinct if and only if the basic reproduction number $\bar{\mathcal{R}}$ of the time-average systems (the autonomous systems obtained by replacing the time-varying parameters with their long-term time averages) is less than 1. Otherwise, $\bar{\mathcal{R}} < 1$ is sufficient but not necessary for extinction. Thus, reducing $\bar{\mathcal{R}}$ of the average system to less than 1 is sufficient to prevent or curtail the spread of an endemic disease.

1. **Introduction.** To understand how to control and eradicate infectious diseases is one of the main goals of mathematical epidemiology. From the study of autonomous models, we know that a disease can cause an epidemic if and only if the basic reproduction number $\mathcal{R}_0$ (the expected number of secondary cases caused by a primary case in a fully susceptible population) is greater than 1 (van den Driessche and Watmough, 2002). Thus to eradicate a disease we need to reduce $\mathcal{R}_0$ to less than 1.

However, many diseases show seasonal behavior (London and Yorke, 1973; Dowell, 2001; Bjornstad et al., 2002; Earn et al., 2002). Seasonality may come from various sources. Seasonally varying transmission rates (Dowell, 2001; Finkenstädt et al., 1998; Dushoff et al., 2004) and fluctuations in birth rates are two common ones. These two factors have been known to cause complex dynamics (Earn et al., 2000; Bauch and Earn, 2003; Finkenstädt and Grenfell, 2000). The mathematical models that describe these diseases are seasonally forced. For such models, $\mathcal{R}_0$ depends on the time of invasion, and thus is a function of time t. To control a disease, must we keep the maximum of $\mathcal{R}_0(t)$ below 1?

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For periodic systems with small oscillation amplitudes, perturbation theory may be used to show that when the amplitude of oscillation of parameters is small, the stability of the disease-free equilibrium (DFE) of the periodic system is determined by the basic reproduction number of the average system, that is, the autonomous system where the time-varying parameters are replaced by their long term averages (Schwartz, 1992). However, when the oscillation amplitude becomes large, it is unclear whether this conclusion remains valid.

In this paper, we will look for extinction conditions for diseases modeled by SEIR (susceptible-exposed-infectious-recovered) models and their variants (Diekmann and Heesterbeek, 2000) with seasonally forced transmission, birth, and death rates.

2. **Models without susceptible recruitment.** An SEIR model without any recruitment of susceptible individuals (from either births or loss of immunity) may be used to describe the short-term spread of diseases with a short course of infection and lifetime immunity (e.g., a specific strain of influenza). It may also be used to study the control of an invading disease, such as the recent SARS epidemic (W.H.O., 2003). In both cases, because of the short time scale, births and deaths may be neglected. For a newly invading disease, loss of immunity can also be ignored because we are interested in the starting phase of the epidemic, at which time the number of infected individuals is small. In this section, we study such a model, with a seasonally forced transmission rate $\beta(t)$ as the only source of seasonality:

$$\dot{S} = -\beta(t)SI\,, \tag{1a}$$

$$\dot{E} = \beta(t)SI - \sigma E\,, \tag{1b}$$

$$\dot{I} = \sigma E - \gamma I\,, \tag{1c}$$

$$\dot{R} = \gamma I\,, \tag{1d}$$

where S, E, I, R are the proportions of the susceptible, latent, infectious and recovered individuals in the population; $\frac{1}{\sigma}$ is the mean latent period; and $\frac{1}{\gamma}$ is the mean infectious period.

If $\frac{\sigma}{\gamma} \gg 1$, the latent period is small compared to the infectious period, so it can be ignored. In this limit, we have an SIR model.

Basic assumptions: here, and throughout this paper, we assume that $\beta(t)$ has nonnegative upper and lower bounds, and the long-term average of $\beta(t)$ exists.

Notation: we denote the long-term average of a function as $\langle\cdot\rangle$; that is,

$$\langle\cdot\rangle = \lim_{t\to\infty} \frac{1}{t}\int_0^t \cdot\, d\tau\,.$$

We can see that the positive octant is invariant because either the boundary hyperplane is invariant ($S = 0$), or, the trajectories point to the inside on the boundary ($E = 0$, $I = 0$ and $R = 0$). If we sum the equations (1), we get $S + E + I + R = 1$ is invariant. Thus, $0 \le S, E, I, R \le 1$.

Because there is no recruitment of S, this model cannot give a sustained epidemic; that is, $I(\infty) = 0$. This may be shown as follows: since $\frac{d}{dt}(S + E + I) = -\gamma I \le 0$, $S + E + I$ is nonincreasing. Note that $S + E + I$ is bounded below by 0. Thus, $S(\infty) + E(\infty) + I(\infty)$ exists. Since $S + E + I$ is a smooth function of t, $\lim_{t\to\infty} \frac{d}{dt}(S + E + I) = \lim_{t\to\infty} -\gamma I(t) = 0$. Thus, $I(\infty) = 0$.

Hence, as for the autonomous model, the disease will disappear if we wait long enough, though a large fraction of the population may have been infected. To control the disease, we want $E + I$ to decrease no matter when the disease is introduced and how many infectious individuals are introduced.

If $\beta(t)$ is a constant β, then we have an autonomous standard SEIR model. For such a model, we know that when $\mathcal{R}_0 = \frac{\beta}{\gamma} < 1$, the number of infectious individuals will decay exponentially; thus, there is no epidemic. On the other hand, if $\mathcal{R}_0 > 1$, the number of infectious individuals will initially grow exponentially—thus, there will be an epidemic.

For time-varying $\beta(t)$, $\frac{\beta(t)}{\gamma}$ can still be interpreted as the basic reproduction number at time t. If there exists a time t_0 such that $\beta(t_0) > \gamma$, and the disease invades around time t_0, then $E + I$ will increase around time t_0 if $S(t_0) \approx 1$. This can be shown as follows. We add up equations (1b) and (1c), and get

$$\frac{d}{dt}(E + I) = \beta(t)SI - \gamma I\,.$$

At any time t_0,

$$\frac{d}{dt}(E + I)|_{t=t_0} = (\beta(t_0)S(t_0) - \gamma)\, I(t_0)\,.$$

Thus, if $\beta(t_0) > \gamma$ and $S(t_0) \approx 1$, $E + I$ increases with t. Because $S \leq 1$, if $\beta(t_0) < \gamma$, $E + I$ decreases with t for all $S(t_0)$.

Hence, if we want $E + I$ to decrease with t for any initial condition, we need

$$\mathcal{R}_{max} = \max_t \left\{ \frac{\beta(t)}{\gamma} \right\} < 1\,,$$

where $\mathcal{R}_{max}$ is in fact the maximum basic reproduction number.

3. **SIR models with recruitment.** If we want to control a disease with a relatively long course of infection, or a disease with temporary immunity that has already been endemic, the recruitment of susceptible individuals from either births or loss of immunity cannot be neglected. From this section on, we study models with recruitment, and look for conditions that prevent epidemics.

Diseases with very short latent period may be described by an SIR model. These models resemble resource-consumer models where the susceptible individuals can be seen as the resource, and the infectious individuals are analogous to the consumer. Hallam and Ma (1986) and Ma and Wang (1997) introduced a method to study the persistence of the consumer species in such models. In this section, we adapt this method to study the eradication threshold condition for SIR models with recruitment.

3.1. **SIR models with births and deaths.** First, we study the model with recruitment from births only. We assume all the new-borns are susceptible, *i.e.,* there is no vertical transmission.

$$\dot{S} = \mu(t) - \mu(t)S - \beta(t)SI\,, \tag{2a}$$

$$\dot{I} = \beta(t)SI - \gamma I - \mu(t)I\,, \tag{2b}$$

$$\dot{R} = \gamma I - \mu(t)R\,, \tag{2c}$$

where $\mu(t)$ is the birth rate at time t; S, I and R are still proportions.

Assumption: $\mu(t)$ has nonnegative upper and lower bounds, and the long-term average $\langle \mu(t) \rangle$ exists.

The positive octant is invariant for this model as well, because either the boundary hyperplane is invariant ($I = 0$), or, the trajectories points to the inside ($S = 0$ and $R = 0$). Given $I(t)$, $R(t)$ is solvable. In fact,

$$R(t) = R(0)e^{-\int_0^t \mu(\tau)d\tau} + \int_0^t e^{-\int_\tau^t \mu(s)ds}\gamma I(\tau)d\tau\,.$$

Thus, we only need to study the first two equations of system (2). If we sum the equations (2), we can see that $S + I + R = 1$ is also invariant. Thus, $S(t), I(t) \geq 0$ and $S + I \leq 1$.

When only a small number of infectious individuals is introduced, the disease cannot invade if and only if the DFE $(1, 0, 0)$ of equations (2) is stable. To study the stability, we linearize system (2) about the DFE:

$$\dot{s} = -\mu(t)s - \beta(t)i\,, \tag{3a}$$

$$\dot{i} = \beta(t)i - \mu(t)i - \gamma i\,. \tag{3b}$$

We can solve $i(t)$ from equation (3b):

$$i(t) = i(0)e^{\int_0^t \beta(\tau)-\mu(\tau)-\gamma d\tau}\,.$$

The stability of $i(t)$ depends on

$$\bar{\mathcal{R}} = \frac{\langle\beta\rangle}{\gamma + \langle\mu\rangle}\,.$$

Specifically, if $\bar{\mathcal{R}} > 1$, then $i(t)$ is unstable; if $\bar{\mathcal{R}} < 1$, then it is stable. To see this, substitute $i(t)$ into equation (3a), and solve for $i(t)$:

$$s(t) = e^{-\int_0^t \mu(\tau)d\tau}\left[s(0) + \int_0^t e^{\int_0^\tau \mu(s)ds}\beta(\tau)i(\tau)d\tau\right]\,.$$

Now note that

$$\begin{aligned}\lim_{t\to\infty} \frac{\int_0^t e^{\int_0^\tau \mu(s)ds}\beta(\tau)i(\tau)d\tau}{e^{\int_0^t \mu(\tau)d\tau}} &= \lim_{t\to\infty} \frac{\frac{d}{dt}\int_0^t e^{\int_0^\tau \mu(s)ds}\beta(\tau)i(\tau)d\tau}{\frac{d}{dt}e^{\int_0^t \mu(\tau)d\tau}} \\ &= \lim_{t\to\infty} \beta(t)i(t)\,.\end{aligned}$$

Thus, for the linear system (3), if $\bar{\mathcal{R}} < 1$, then $i(\infty) = 0$; thus, $s(\infty) = 0$. If $\bar{\mathcal{R}} > 1$, then $i(\infty) = \infty$, thus $s(\infty) = \infty$.

Note that $\bar{\mathcal{R}}$ is indeed the basic reproduction number of the average system. Hence we have the following.

Theorem 1. *The stability of the DFE of the system* (2) *is the same as that of the average system; that is,the DFE is unstable if the basic reproduction number of the average system* $\bar{\mathcal{R}} = \frac{\langle\beta\rangle}{\gamma+\langle\mu\rangle} > 1$*, stable if* $\bar{\mathcal{R}} < 1$.

This theorem ensures that if $\bar{\mathcal{R}} < 1$, then the disease cannot invade a population when only a small number of infectious individuals are introduced. If a large number of infected individuals are introduced, can the disease become endemic even if we bring the $\bar{\mathcal{R}}$ below 1? The following theorem answers this question.

Theorem 2. *When* $\bar{\mathcal{R}} < 1$*, for all* $I(0) > 0$, $I(\infty) = 0$.

Proof. We divide by I on both sides of (2b):

$$\frac{dI/dt}{I} = \frac{d}{dt}\ln I(t) = \beta(t)S - \gamma - \mu(t)\,.$$

Since $S \le 1$, we have

$$\frac{d}{dt}\ln I(t) \le \beta(t) - \gamma - \mu(t)\,.$$

We take long-term average with respect to t on both sides, and get, as $t \gg 1$,

$$\frac{\ln I(t) - \ln I(0)}{t} \le \langle\beta\rangle - \gamma - \langle\mu\rangle\,.$$

Hence, we have

$$I(t) < I(0)e^{(\langle\beta\rangle-\gamma-\langle\mu\rangle)t}\,.$$

When $\bar{\mathcal{R}} < 1$, $\langle\beta\rangle - \gamma - \langle\mu\rangle < 0$. Thus, $I(\infty) = 0$.

□

This theorem shows that as long as $\bar{\mathcal{R}} < 1$, the disease will not become endemic not matter how many infectious individuals are initially introduced.

Note that generally, $\bar{\mathcal{R}}$ is not the mean basic reproduction number of system (1); that is, $\bar{\mathcal{R}} \neq \langle\frac{\beta(t)}{\gamma+\mu(t)}\rangle$, unless $\mu(t)$ is a constant function. $\bar{\mathcal{R}}$ is only the basic reproduction number of the time-average system.

3.2. **Disease-induced mortality.** Without deaths caused by the disease, the population dynamics is always independent of the epidemic process. However, when such "excess deaths" cannot be neglected, the population dynamics will be coupled with the epidemic process. In this subsection, we explore the SIR model with excess deaths.

Suppose $b(t)$ and $d(t)$ are the birth and natural death rates. Let $N(t)$ be the population size at time t. Without the disease, the population dynamics are governed by

$$\dot{N} = b(t)N - d(t)N\,.$$

Let X, Y, and Z be the number of susceptible, infectious and recovered individuals in the population. Thus

$$X + Y + Z = N\,. \tag{4}$$

Let α be the disease-induced death rate. Then, under the influence of the disease, the population dynamics become

$$\dot{N} = b(t)N - d(t)N - \alpha Y\,. \tag{5a}$$

In terms of X, Y, Z and N, the epidemic process becomes

$$\dot{X} = b(t)N - d(t)S(t) - \frac{\beta(t)}{N}XY\,, \tag{5b}$$

$$\dot{Y} = \frac{\beta(t)}{N}XY - \gamma Y - \alpha Y - d(t)Y\,, \tag{5c}$$

$$\dot{Z} = \gamma Y - d(t)Z\,, \tag{5d}$$

Note that to make the units correct, the transmission term becomes $\frac{\beta(t)}{N}XY$. We will show that this term is indeed equivalent to the $\beta(t)SI$ term in the above models.

Naturally, we want to rewrite system (5) into a system of proportions $S = \frac{X}{N}$, $I = \frac{Y}{N}$, and $R = \frac{Z}{N}$:

$$\dot{N} = N(t)[b(t) - d(t) - \alpha I]\,, \tag{6a}$$

$$\dot{S} = b(t) - b(t)S - \beta(t)SI + \alpha SI\,, \tag{6b}$$

$$\dot{I} = \beta(t)SI - \gamma I - \alpha I - b(t)I + \alpha I^2\,, \tag{6c}$$

$$\dot{R} = \gamma I - b(t)R + \alpha IR\,. \tag{6d}$$

Note that there are nonlinear positive feedbacks induced by α. This is because at any time individuals die from the disease, the population size decreases; thus, the proportions of each class of individuals increase. However, we should see that when $\alpha = 0$, system (6) becomes system (2), if we denote $\mu(t) = b(t)$. We can also see that the natural death rate $d(t)$ does not affect the proportions S, I, and R. Furthermore, the transmission term in equations (5) is indeed equivalent to those in the models in previous sections.

From equation (4), we have $S + I + R \equiv 1$. Furthermore, as in the arguments in section 3.1, we can show that the positive octant is invariant. Thus, $S(t) < 1$, $I(t) < 1$, and $S + I \leq 1$ for all t.

Equations (6b) and (6c) are independent of equations (6a) and (6d). If we know the solutions to S and I, then we can solve for N and R. Thus we only consider equations (6b) and (6c).

To find the invasion threshold, we again study the local stability of the system at the DFE ($S = 1, I = 0$). We linearize system (6) about the DFE:

$$\dot{s} = -b(t)s - \beta(t)i + \alpha i\,, \tag{7a}$$

$$\dot{i} = \beta(t)i - \gamma i - \alpha i - b(t)i\,. \tag{7b}$$

Although the linear system, (7), is slightly different from system (3), the arguments leading to Theorem 1 are still valid. Hence, we have the following.

Theorem 3. *The stability of the DFE of system* (6) *is the same as that of the average system; that is,if the basic reproduction number of the average system* $\bar{\mathcal{R}} = \frac{\langle\beta\rangle}{\gamma+\alpha+\langle b\rangle} > 1$*, the DFE is unstable. If* $\bar{\mathcal{R}} < 1$*, the DFE is stable.*

Will the positive feedbacks induced by α change the global stability of the DFE? Specifically, if $I(0)$ is large, will the disease persist even if $\bar{\mathcal{R}} < 1$? Because $S+I \leq 1$, from equation (6c) we have

$$\dot{I} \leq \beta(t)I(1 - I) - \gamma I - \mu(t)I - \alpha I + \alpha I^2\,.$$

Thus $I(t) \leq w(t)$, where $w(t)$ is the solution of

$$\dot{w} = \beta(t)w(1 - w) - \gamma w - \mu(t)w - \alpha w + \alpha w^2\,, \tag{8}$$

with the initial condition $w(0) = I(0)$. Luckily, equation(8) is a Bernoulli equation, so we can solve it explicitly. We let $u = \frac{1}{w}$, then

$$\dot{u} = -[\beta(t) - \gamma - \mu(t) - \alpha]u + [\beta(t) - \alpha]\,.$$

This is a linear equation in u. Let $f(t) = \beta(t) - \gamma - \mu(t) - \alpha$,

$$u(t) = \left[u(0) + \int_0^t e^{\int_0^\tau f(s)ds}[\beta(\tau) - \alpha]d\tau\right] e^{-\int_0^t f(s)d\tau}\,. \tag{9}$$

When $\bar{\mathcal{R}} < 1$, $\lim_{t\to\infty} \int_0^t f(\tau)d\tau = -\infty$; thus,

$$\int_0^\infty e^{\int_0^t f(\tau)d\tau}[\beta(t)-\alpha]dt = \int_0^\infty e^{\int_0^t f(\tau)d\tau} f(t)dt + \int_0^\infty e^{\int_0^t f(\tau)d\tau}[\mu(t)+\gamma]dt\,,$$
$$= -1 + \int_0^\infty e^{\int_0^t f(\tau)d\tau}[\mu(t)+\gamma]dt\,.$$

Now substitute the above equation into equation (9), and note that $u(0) = \frac{1}{w(0)} = \frac{1}{I(0)} > 1$. Thus, for $t \gg 1$,

$$u(t) \geq e^{-\int_0^t f(\tau)d\tau} \int_0^\infty e^{\int_0^t f(\tau)d\tau}[\mu(t)+\gamma]dt\,.$$

Thus, when $\bar{\mathcal{R}} < 1$, $u(\infty) = \infty$, $I(\infty) = \frac{1}{u(\infty)} = 0$. We have the following.

Theorem 4. *For the system* (6)*, when* $\bar{\mathcal{R}} < 1$*, for all* $I(0) < 1$*,* $I(\infty) = 0$.

3.3. **Loss of immunity: SIS and SIRS models.** In this subsection we study SIR models with the recruitment of the susceptibles from the loss of immunity. We assume that recovered individuals lose immunity and reenter the susceptible class S as a fixed rate ρ. For simplicity, we ignore births and deaths in this model:

$$\dot{S} = -\beta(t)SI + \rho R\,, \tag{10a}$$
$$\dot{I} = \beta(t)SI - \gamma I\,, \tag{10b}$$
$$\dot{R} = \gamma I - \rho R\,. \tag{10c}$$

Summing the equations, we find that $S + I + R = 1$ is invariant.

When $\rho = 0$, we have an SIR model. When $\frac{\rho}{\gamma} \gg 1$, the immune stage R may be ignored. In this limit, we have an SIS model. S and I are proportions; thus, for SIS models, we have $S+I = 1$. Hence, the SIS models are intrinsically one-dimensional. In fact, it can be written as

$$\dot{I} = \beta(t)(1-I) - \gamma I\,.$$

This is a Bernoulli equation, which is solvable. In fact,

$$I(t) = \frac{I(0)e^{\int_0^t \beta(\tau)d\tau - \gamma t}}{1 + I(0)\int_0^t \beta(\tau)e^{\int_0^\tau \beta(s)ds - \gamma\tau}d\tau}\,.$$

Thus $I(\infty) = 0$ if and only if $\bar{\mathcal{R}} = \frac{\langle\beta\rangle}{\gamma} < 1$.

Will ρ affect the result? Let us study the stability of the DFE of the system (10). We linearize the system about the DFE:

$$\dot{s} = -\rho s - \beta(t)i + \rho r\,, \tag{11a}$$
$$\dot{i} = [\beta(t) - \gamma]i\,, \tag{11b}$$
$$\dot{r} = \gamma i - \rho r\,. \tag{11c}$$

The linear system (11) is solvable. In fact, equation (11b) is independent. We can solve for $i(t)$:

$$i(t) = i(0)e^{-\int_0^t \beta(\tau)d\tau - \gamma t}\,.$$

Thus, for the liner system (11), $I(\infty) = 0$ if $\bar{\mathcal{R}} = \frac{\langle\beta\rangle}{\gamma} < 1$; $I(\infty) = \infty$ if $\bar{\mathcal{R}} > 1$. We can then substitute $i(t)$ into equations (11c) and (11a) and solve for $r(t)$ and $s(t)$. We can show that $r(\infty) = s(\infty) = 0$ if $i(\infty) = 0$; $r(\infty) = s(\infty) = \infty$ if $i(\infty) = \infty$. Thus, we have the following.

Theorem 5. *The DFE of the system* (10) *is unstable if* $\bar{\mathcal{R}} = \frac{\langle\beta\rangle}{\gamma} > 1$, *stable if* $\bar{\mathcal{R}} < 1$.

Furthermore, the arguments leading to Theorem 2 also apply to system (10). Hence, we have the following.

Theorem 6. *For system* (10), $I(\infty) = 0$ *for all* $I(0) > 0$ *if* $\bar{\mathcal{R}} < 1$.

Note that $\bar{\mathcal{R}}$ is the basic reproduction number of their average system.

We can also consider the SIRS model with births, natural deaths, and disease-induced deaths:

$$\dot{S} = \mu - \mu S - \beta(t)SI + \rho R + \alpha SI\,, \tag{12a}$$

$$\dot{I} = \beta(t)SI - \gamma I - \mu I - \alpha I + \alpha I^2\,, \tag{12b}$$

$$\dot{R} = \gamma I - \rho R - \mu R + \alpha IR\,. \tag{12c}$$

With the same arguments leading to Theorem 3 and 4, we have the following.

Theorem 7. *The DFE of the system* (12) *is stable if* $\bar{\mathcal{R}} = \frac{\langle\beta\rangle}{\gamma+\alpha+\langle\mu\rangle} < 1$, *unstable if* $\bar{\mathcal{R}} > 1$. *Furthermore, for all* $I(0) > 0$, $I(\infty) = 0$ *if* $\bar{\mathcal{R}} < 1$.

Thus, for SIR models with recruitment of susceptible individuals, the disease will be eradicated if and only if the basic reproduction number $\bar{\mathcal{R}}$ of their average system is less than 1.

4. **SEIR models with recruitment from loss of immunity.** Diseases such as HIV/AIDS and tuberculosis have latent stages that last for many years. For such diseases, ignoring the latent period as we did in section 3 may be inappropriate. In this section, we study an SEIR model with recruitment from the loss of immunity. For simplicity, we ignore births and deaths:

$$\dot{S} = -\beta(t)SI + \rho R\,, \tag{13a}$$

$$\dot{E} = \beta(t)SI - \sigma E\,, \tag{13b}$$

$$\dot{I} = \sigma E - \gamma I\,, \tag{13c}$$

$$\dot{R} = \gamma I - \rho R\,. \tag{13d}$$

Naturally, with the results of section 3, we would expect that the basic reproduction number $\bar{\mathcal{R}} = \frac{\langle\beta\rangle}{\gamma}$ of the average system gives the eradication threshold. However, this is not true. For example, if $\beta(t) = 1 + 0.8\sin(t)$, $\rho = 1$, $\gamma = 0.99$, $\sigma = 0.3$, then $\bar{\mathcal{R}} = \frac{1}{0.99} > 1$, but figure 1 shows that $I(t)$ of the solution starting from $(0.99, 0, 0.01, 0)$ goes to 0.

But still, the eradication condition is related to the linear stability of the DFE $(1, 0, 0, 0)$. To study this stability, we linearize system (13) about the DFE:

$$\dot{s} = -\beta(t)i + \rho r\,, \tag{14a}$$

$$\dot{e} = \beta(t)i - \sigma e\,, \tag{14b}$$

$$\dot{i} = \sigma e - \gamma i\,, \tag{14c}$$

$$\dot{r} = \gamma i - \rho r\,. \tag{14d}$$

Thus, from equation (14d) we have $r(\infty) = 0$ if and only if $i(\infty) = 0$. Then from equation (14a) we know $s(\infty) = 0$ if and only if $i(\infty) = r(\infty) = 0$. Thus, the

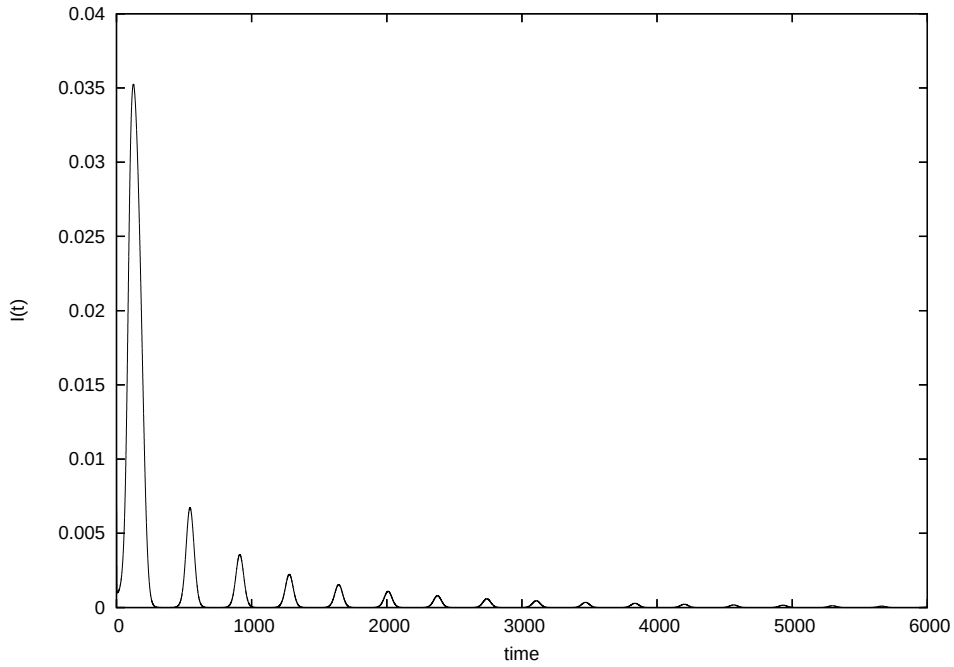

FIGURE 1. $I(t)$ component of the solution to the SEIRS model (13), where $\beta(t) = 1 + 0.8\sin(t)$, $\gamma = 0.98$, $\sigma = 0.3$, $\rho = 1$. Even though the basic reproduction number of the average system is $\bar{\mathcal{R}} = \frac{1}{0.98} > 1$, $I(t)$ goes to 0.

stability of the linear system (14) is determined by the two equations (14b) and (14c).

Let $w = \frac{e}{i}$. Then, equation (14c) becomes

$$\dot{i} = \sigma w i - \gamma i \,.$$

Thus, $i(\infty) = 0$ if and only if $\frac{\sigma\langle w\rangle}{\gamma} < 1$. Can we compute $\langle w\rangle$?

$$\begin{aligned} \dot{w} &= \frac{\dot{e}}{i} - \frac{\dot{i}}{i}\frac{e}{i}\,, \\ &= \beta(t) - \sigma\frac{e}{i} - (\sigma\frac{e}{i} - \gamma)\frac{e}{i}\,. \end{aligned}$$

Hence, we have

$$\dot{w} = \beta(t) - (\sigma - \gamma)w - \sigma w^2\,. \tag{15}$$

Unfortunately this is not solvable. But we know w is bounded, because when $w \gg 1$, $\frac{d}{dt}w < 0$; when $w = 0$, $\frac{d}{dt}w = \beta(t) \geq 0$. We take the long-term average on both sides of equation (15):

$$\begin{aligned} \lim_{t\to\infty}\frac{w(t) - w(0)}{t} &= 0\,, \\ &= \langle\beta\rangle - (\sigma - \gamma)\langle w\rangle - \sigma\langle w^2\rangle\,, \\ &\leq \langle\beta\rangle - (\sigma - \gamma)\langle w\rangle - \sigma\langle w\rangle^2\,. \end{aligned}$$

Hence,

$$\langle w\rangle \le \frac{\gamma-\sigma+\sqrt{(\sigma-\gamma)^2+4\langle\beta\rangle\sigma}}{2\sigma}\,.$$

Thus, $\frac{\langle\beta\rangle}{\gamma}<1$ implies that $\langle w\rangle<\frac{\gamma}{\sigma}$, *i.e.,* $\frac{\sigma\langle w\rangle}{\gamma}<1$. Hence, we have the following.

Theorem 8. *If the basic reproduction number* $\bar{\mathcal{R}}=\frac{\langle\beta\rangle}{\gamma}$ *of the average system is less than 1, then the DFE of system* (13) *is locally asymptotically stable.*

Will $I(t)$ converge to 0 for all $I(0)\ge 0$ when $\bar{\mathcal{R}}<1$? To answer this question, we only need to show that the solutions to system (13) are bounded by the solutions to linear system (14) with the same initial conditions. Let E', I' be the solutions to equations (14b) and (14c), and $E'(0)=E(0)$, $I'(0)=I(0)$, $\Delta E=E-E'$, $\Delta I=I-I'$. Thus, $\Delta E(0)=\Delta I(0)=0$. Then we have

$$\Delta\dot{E}=\beta(t)\Delta I-\sigma\Delta E+\beta(t)(S-1)I\,, \tag{16a}$$

$$\Delta\dot{I}=\sigma\Delta E-\gamma\Delta I\,. \tag{16b}$$

This is a nonhomogeneous linear system, with the homogeneous part being equations (14b) and (14c). Let $\Phi(t)$ be the fundamental solution to equations (14b) and (14c), then

$$\begin{pmatrix} E' \\ I' \end{pmatrix}=\Phi(t)\begin{pmatrix} E(0) \\ I(0) \end{pmatrix}.$$

Since the positive quadrant is invariant for system (14b, 14c), we have $\Phi(t)>0$ for all t. We solve equations (16):

$$\begin{pmatrix} \Delta E \\ \Delta I \end{pmatrix}=\int_0^t \Phi(t-\tau)\begin{pmatrix} \beta(t)(S-1)I \\ 0 \end{pmatrix}d\tau\,.$$

Since $S\le 1$, $\Phi(t)>0$, we have $\Delta E<0$, $\Delta I<0$. In other words, $I(t)<I'(t)$. But $I(t)\ge 0$. Thus, if $I'(\infty)=0$, we have $I(\infty)=0$. Hence, we have the following.

Theorem 9. *For equations* (13)*, when* $\bar{\mathcal{R}}=\frac{\langle\beta\rangle}{\gamma}<1$*, for all* $I(0)>0$*,we have* $I(\infty)=0$*.*

5. **Conclusions and discussion.** For seasonally forced epidemic models, the basic reproduction number $\mathcal{R}_0$ is a function of invasion time. The eradication threshold condition $\max_t\{\mathcal{R}_0(t)\}<1$ is useful if we are attempting to eradicate an emerging disease. SEIR models without recruitment of susceptibles can usually be used in such cases. This threshold condition ensures that $E+I$ will always decrease, no matter when and how the disease is introduced. Thus, there will be no outbreak, or an outbreak that has begun will be curtailed. When a threatening disease appears, we may wish to fight its spread at any cost, as in the recent SARS epidemic. However, it may be unrealistic or too costly to enforce this condition for a long time, especially if the disease becomes endemic.

To model endemic diseases, we need to use models with recruitment. In this case, we are usually interested in controlling the disease in the long term, rather than preventing outbreaks altogether. We can instead make the outbreaks decrease in size. If the latent period can be neglected, then this can be achieved by reducing the basic reproduction number $\bar{\mathcal{R}}$ of the average system to less than 1. In fact, this condition is necessary and sufficient for the extinction of the disease, no matter what the initial conditions are.

If the latent period cannot be neglected, then $\bar{\mathcal{R}} < 1$ is not necessary for eradication, but it is still sufficient. We can always compute the sufficient and necessary condition by solving equation (15) numerically. However, it is impossible to obtain an analytical threshold condition, because it would be equivalent to solving equation (15) analytically.

Our main conclusion is that whenever an endemic disease can be modeled by a variant of an SEIR model, to eradicate the infection, it is sufficient to bring the basic reproduction number of the average system below 1.

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