Seasonality

N. Bacaër, Mathématiques et épidémies, Éditions Cassini 2021

W. Wang, X-Q Zhao, Threshold dynamics for compartmental epidemic models in periodic environments, J. Dyn. Diff. Equ. (2008) 20: 699-717

H. R. Thieme, see P 3.11 and Renewal theorems for linear periodic Volterra Integral Equations, J. Int. Equa. (1984) 253-277

H. Inaba, Age-Structured Population Dynamics in Demography and Epidemiology, Springer, 2017.

$$\frac{dS}{dt} = -FS \qquad F(t) = \int_0^\infty A(t,\tau) \begin{Bmatrix} -\frac{dS}{dt}(t-\tau) \\ F(t-\tau)S(t-\tau) \end{Bmatrix} d\tau$$

Note: when we integrate F, interchanging the integrals is now not of much help, since A also depends on t.

So we write

$$F(t) = N \int_0^\infty A(t,\tau) F(t-\tau) e^{-\int_{-\infty}^{t-\tau} F(\sigma)\,d\sigma} d\tau$$

which is a scalar RE for the f-o-i F. Its linearization reads

$$y(t) = N \int_0^\infty A(t,\tau)\, y(t-\tau)\, d\tau$$

The Ansatz $y(t) = e^{\lambda t}\psi(t)$ leads to

$$\psi(t) = N \int_0^\infty A(t,\tau)\, e^{-\lambda\tau}\, \psi(t-\tau)\, d\tau$$

Here we assume that A is periodic in the first variable and that ψ is periodic with the same period.

We write

$$\psi = K_\lambda \psi$$

and call K_0 the NGO and the spectral radius of K_0 we call the Basic Reproduction Number R_0.

But how does this relate to the interpretation and to the formalism introduced on P3.g? In the generation way of looking at population growth, we presume that it does **not** matter **when** offspring is produced. But when environmental conditions vary, it **does** matter.

To solve this problem of interpretation, we label newly infected individuals by the time, modulo the period, at which they became infected. To simplify the notation, we take the length of the period as the unit of time. We introduce

$$\tilde{A}(\tau,t,s) = A(t,\tau)\,\delta\big(t-[s+\tau]\big), \quad 0\le t<1, \quad 0\le s<1$$

with

$$[s+\tau] := s+\tau \pmod 1, \quad \text{normalized by } 0\le [s+\tau]<1$$

The underlying idea is that an individual, that became infected at phase s exactly τ units of time ago, creates offspring with phase $[s+\tau]$. In this setting, the NGO is given by (cf. P3.g; let Φ have uniform density)

$$(K_0\psi)(t) = N\int_0^1\Big(\int_0^\infty \tilde{A}(\tau,t,s)\,d\tau\Big)\psi(s)\,ds$$

Now use

$$\int_0^\infty \tilde{A}(\tau,t,s)\,d\tau = \begin{cases} \sum_{k=0}^{\infty} A(t,t-s+k), & t>s \\ \sum_{k=1}^{\infty} A(t,t-s+k), & t<s \end{cases}$$

and ~~with~~ a bit of formula manipulation to check that this corresponds exactly to K_0 as defined above.

Recall that on P 2.1 we explained how compartmental models are included in this formalism for the autonomous (= time translation invariant) situation. The analogue for the present non-autonomous situation is

$$A(t,\tau) = U(t)\, \Phi_\Sigma(t, t-\tau)\, V(t-\tau)$$

where $\Phi_\Sigma(t,s)$ is the fundamental matrix solution of the linear problem

$$\frac{du}{dt}(t) = \Sigma(t)\, u(t)$$

with Σ a periodic matrix function of time.

Define

$$x(t) = \int_{-\infty}^{t} \Phi_\Sigma(t,\sigma)\, V(\sigma)\, F(\sigma)\, S(\sigma)\, d\sigma$$

then

$$\frac{dx}{dt}(t) = \Sigma(t)\, x(t) + F(t)\, S(t)\, V(t)$$

$$F(t) = U(t)\, x(t)$$

$$\frac{dS}{dt}(t) = -F(t)\, S(t)$$

is the corresponding compartmental ODE system.

The linearized system reads

$$\frac{dx}{dt}(t) = \Sigma(t)\, x(t) + T(t)\, x(t)$$

where

$$T(t)\, x = N(U(t)x)\, V(t)$$

The eigenvalue problem $K_0 \psi = \lambda \psi$ can of course be written as $\psi = \frac{1}{\lambda} K_0 \psi$

and if we put $\psi(t) = U(t)x(t)$ we obtain that x should satisfy

$$x'(t) = \Sigma(t)x(t) + \frac{1}{\lambda}T(t)x(t)$$

and be periodic. This shows

i) that R_0 informs us about the control effort, in terms of reduction of transmission, needed to prevent or stop an outbreak

ii) that we can determine R_0 by, for instance numerically, finding a positive λ such that the dominant Floquet multiplier of the above system equals 1, cf. Wang & Zhao, see Ps.1.

For a good understanding of the dynamics under periodic environmental conditions, numerical experiments are indispensable, cf. Bacaër, Ps.1. On P1.10 we formulated a higher order nonlinear recurrence relation for a (scalar) function s of discrete time t. We now formulate a nonlinear system of equations that incorporates the time dependence of the coefficients. To simplify the presentation, we make the reasonable assumption

$$A(t,\tau) = a(t)b(\tau)$$

Let

$$X_1(t) = s(t) = \frac{S(t)}{N}$$

$$X_2(t) = s(t-1) - s(t) = \text{incidence at time point } t$$

$$X_j(t) = X_{j-1}(t-1) \text{ for } j \geq 3$$

then

$$X_1(t+1) = X_1(t)\, e^{-a(t)\sum_{j=1}^{m} b_j X_{j+1}(t)}$$

$$X_2(t+1) = X_1(t)\left(1 - e^{-a(t)\sum_{j=1}^{m} b_j X_{j+1}(t)}\right)$$

$$X_j(t+1) = X_{j-1}(t), \quad j \geq 3$$

(Note that one should replace $a(t)$ by some average value if a changes considerably during one time step.) (Ps.5)

Preliminary conclusion: from a theoretical point of view, not that much changes when we incorporate periodicity, but things become a bit less explicit and a bit more complicated. We now add a few observations to illustrate that, from a more practical, inference oriented, point of view, subtle new issues arise.

Observation 1: Replacing periodic coefficients by their average value (to obtain an autonomous system) may lead to wrong conclusions. If in the SIR and SEIR systems we allow β to be periodic, then for the linearized SIR system we find

$$I(t) = I(0)\, e^{\int_0^t (\beta(\sigma) N - \alpha)\, d\sigma}$$

and conclude that (in)stability is governed by the sign of $\bar{\beta} N - \alpha$ with $\bar{\beta} := \frac{1}{p}\int_0^p \beta(\sigma)\, d\sigma$ and p the period. So here averaging does give the right answer. But the reason is that scalar variables commute. Matrices, on the other hand, do not necessarily commute. Recall $\Phi_\Sigma(t,s)$ as introduced on Ps.3. In general

$$\Phi_\Sigma(t,s) \neq e^{\int_s^t \Sigma(\sigma)\, d\sigma}$$

In the SEIR case the linearized system reads

$$\begin{aligned} \frac{dE}{dt} &= \beta(t) N I - \gamma E \\ \frac{dI}{dt} &= \gamma E - \alpha I \end{aligned}$$

We may now contrast the case in which β is constant, say $\bar{\beta}$, (so for which $R_0 = \frac{\bar{\beta} N}{\alpha}$) with the case where β is mostly zero, but equal to $\frac{1}{\varepsilon}\bar{\beta}$ on a small interval of length ε.

Exercise Convince yourself that the stability conditions for these two cases are different, even though β has the same average.

Side-remark In the ODE book of J.K. Hale you can find an example, due to Markus and Yamabe, of a periodic matrix $M(t)$ such that for every fixed t all eigenvalues of $M(t)$ have strictly negative real part and yet one of the Floquet multipliers is (real and) bigger than one.

Observation 2 In the paper "On the final size of epidemics with seasonality" (Bull. Math. Biol. (2009) 71: 1954 -1966), N. Bacaër and M.G.M. Gomes show that timing and size of the initiation of an outbreak can have quite some impact on the final size. Also, fixing the initiation, but changing $\beta(t)$ such that R_0 increases, may lead to a decrease of the final size. This at first counterintuitive result is, in a sense, caused by a reduction of the overshoot phenomenon, cf. P1.5, when β goes through a trough immediately after reaching the HIT.

Temporary Immunity

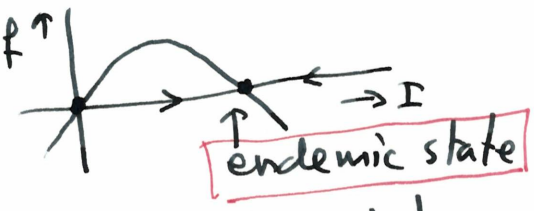
SIS (e.g., Gonorrhea)

$$\dot{S} = -\beta SI + \alpha I$$

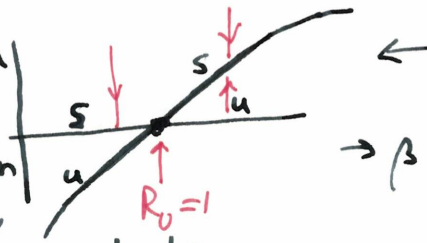
$$S + I = N \qquad \dot{I} = \beta SI - \alpha I$$

$$\dot{I} = f(I) \text{ with } f(I) = (\beta N - \alpha - \beta I)I$$

$$R_0 = \frac{\beta N}{\alpha} > 1 \Rightarrow$$



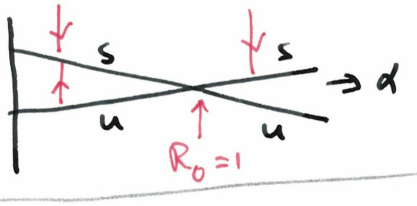
Note: in the endemic state $\bar{s} = \frac{S}{N} = \frac{1}{R_0}$ so $R_{eff} = 1$ and the state is at the HIT



← NB here s means stable, not susc., and u means unstable

Transcritical bifurcation
Exchange of Stability
Supercritical branch is stable
The interpretation requires states to be positive

In terms of "control" variable / parameter α:



Modeling Considerations

1. Susceptibility may **not** return **immediately** after the infectious period has ended
2. Not necessarily "all or nothing". There may be **partial protection** / reduced susceptibility. Recall the vaccination story on P3.3: reduction may concern the susceptibility or the infectiousness (given reinfection) or both.
3. From a clinical perspective, **reduction of illness** is important, not just reduction of the contribution to the transmission cycle.
4. Reinfection may **boost** immunity, without causing illness or infectiousness.

We now present an example of a general fact:

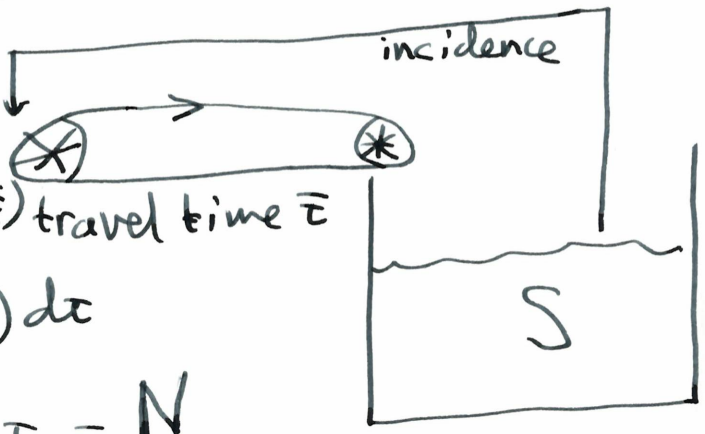
delayed negative feedback can cause oscillations

G. Gripenberg, Periodic solutions of an epidemic model, J. Math. Biol. (1980) 10: 271–280

O. Diekmann, R. Montijn, Prelude to Hopf bifurcation in an epidemic model: analysis of a characteristic equation associated with a nonlinear Volterra integral equation, J. Math. Biol. (1982) 14: 117–127

Chapter XI of O. Diekmann, S. A. van Gils, S. M. Verduyn-Lunel, H-O. Walther, Delay Equations: Functional, Complex and Nonlinear Analysis, Springer, 1995 is devoted to the analysis of characteristic equations

In "Numerical bifurcation analysis of renewal equations via pseudospectral approximation, F. Scarabel, O. Diekmann, R. Vermiglio, J. Comp. Appl. Math. (2021) 397: 113611" the equation studied below is treated as a test problem, see Section 2.1.



$$\frac{dS}{dt}(t) = -F(t)S(t) + F(t-\bar\tau)S(t-\bar\tau)$$

$$F(t) = \int_0^{\bar\tau} A(\tau)F(t-\tau)S(t-\tau)\,d\tau$$

$$S(t) + \int_0^{\bar\tau} F(t-\tau)S(t-\tau)\,d\tau = N$$

We combine these three equations into one equation for the incidence:

$$F(t)S(t) = \int_0^{\bar\tau} A(\tau)F(t-\tau)S(t-\tau)\,d\tau \left(N - \int_0^{\bar\tau} F(t-\tau)S(t-\tau)\,d\tau\right)$$

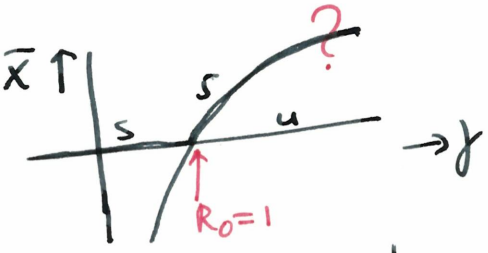
Scaling: $x(t) := \frac{\bar\tau}{N} F(\bar\tau t)S(\bar\tau t)$ $\qquad \tau := \bar\tau\sigma$

assume b is bounded $\rightarrow$ $b(\sigma) := \dfrac{\bar\tau A(\bar\tau\sigma)}{\bar\tau\int_0 A(\tau)\,d\tau}$ $\qquad \gamma := N\int_0^{\bar\tau} A(\tau)\,d\tau \leftarrow = R_0$

Recall the notation $x_t(\theta) = x(t+\theta)$, cf. P2.9

$x(t) = F(x_t)$ with $F(\phi) := \gamma\left(1 - \int_0^1 \phi(-\sigma)d\sigma\right)\int_0^1 b(\sigma)\phi(-\sigma)d\sigma$

steady states



disease free : $\bar{x}_1 = 0$

endemic : $\bar{x}_2 = 1 - \frac{1}{\gamma}$

observe : in the endemic state $\bar{s} = 1 - \bar{x} = \frac{1}{\gamma} = \frac{1}{R_0}$

Observe : $F : L_1 \to \mathbb{R}$ is differentiable, since it is a smooth nonlinear function of two bounded linear functionals

$$DF(\bar{x})\phi = -\gamma\bar{x}\int_0^1 \phi(-\sigma)d\sigma + \gamma(1-\bar{x})\int_0^1 b(\sigma)\phi(-\sigma)d\sigma$$

Linearized equation : $y(t) = DF(\bar{x})y_t$

Ansatz : $y(t) = e^{\lambda t}$

$\Rightarrow 1 = DF(\bar{x})e^{\lambda\cdot}$ (since $e^{\lambda(t+\theta)} = e^{\lambda t}e^{\lambda\theta}$ and $DF(\bar{x})$ is linear)

Characteristic equation

$$1 = -\gamma\bar{x}\frac{1-e^{-\lambda}}{\lambda} + \gamma(1-\bar{x})\hat{b}(\lambda)$$

① $\gamma\hat{b}(\lambda) = 1$ ② $\hat{b}(\lambda) + (1-\gamma)\frac{1-e^{-\lambda}}{\lambda} = 1$

Both have root $\lambda = 0$ for $\gamma = 1$. If γ increases, the root of ① moves from the lhp to the rhp (and all other roots are, for $\gamma - 1$ small, in the lhp. A simple computation shows that the zero root of ② moves in the opposite direction. For $\gamma - 1$ positive but small, all roots of ② are in the lhp. According to the Principle of Linearized Stability (cf. references on P2.10), the steady state $\bar{x}_2$ is then asymptotically stable. But how about larger values of γ?

By considering the left hand side of equation ② for $\mathrm{Re}\,\lambda \to \infty$ we see that roots cannot enter the rhp of $\mathbb{C}$ from the far right when γ varies. According to the Lemma of Riemann-Lebesgue, they can neither enter from high up (note that roots occur in complex conjugate pairs, so "high up" and "deep down" occur simultaneously, if at all). So if the steady state $\bar{x}_2$ becomes unstable, it does so by a couple of conjugate roots passing the imaginary axis (since $\lambda = 0$ cannot be a root for $\gamma \neq 1$). In other words, we want to know whether or not $\bar{x}_2$ undergoes a Hopf bifurcation when γ is increased.

Side remark: See "A didactical note on the advantage of using two parameters in Hopf bifurcation studies, O. Dieckmann, K. Korvasová, J. Biol. Dyn. (2013) 7 (Suppl. 1): 21-30" for a plea to use two parameters when embarking on such an investigation. It so happens that for the present problem a one-parameter study works well.

Exercise Use the IFT (Implicit function theorem) to prove that ② has roots which converge to $\pm 2k\pi i$ for $\gamma \to \infty$ and that they do so from the rhp when $b_k > 0$ and from the lhp when $b_k < 0$, where

$$b_k := 2\int_0^1 b(\tau)\sin(2\pi k\tau)\,d\tau$$

See the second reference on Ps.8 for

Theorem As γ increases from 1 to ∞, exactly as many pairs of roots of ② cross the imaginary axis, as there are $k \in \mathbb{N}$ for which $b_k > 0$. These are simple and go from left to right with positive speed. The positive imaginary axis is passed in the interval $((2k-1)\pi, 2k\pi)$

Observation $b_1 > 0$ if the support of b is contained in $[0, \frac{1}{2}]$