Environmentally Transmitted Pathogens

ODE models

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Paper series worth reading

Model here is a particular case in

- Kermack & McKendrick. A contribution to the mathematical theory of epidemics (1927)

That paper was followed by a series of "Contributions to the mathematical theory of epidemics."

- II. The problem of endemicity (1932)
- III. Further studies of the problem of endemicity (1933)
- IV. Analysis of experimental epidemics of the virus disease mouse ectromelia (1937)
- V. Analysis of experimental epidemics of mouse-typhoid; a bacterial disease conferring incomplete immunity (1939)

What is the size of an epidemic?

- If we are interested in the possibility that an epidemic occurs
  - Does an epidemic peak always take place?
  - If it does take place, what is its size?

- If an epidemic traverses a population, is everyone affected/infected?

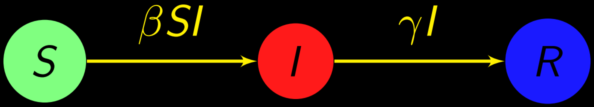
The SIR model without demography

- The period of time under consideration is sufficiently short that demography can be neglected (we also say the model has *no vital dynamics*)
- Differs from the SIS model, which includes demography (although it does consider it as being constant)
- As in SIS model, individuals are either *susceptible* to the disease or *infected* (and *infectious*) by the disease
- However, after recovering or dying from the disease, individuals are *removed* from the infectious compartment (R)
- Incidence is of **mass action** type, βSI

The Kermack-McKendrick model

This model is typically called the Kermack-McKendrick (KMK) SIR model

$$S' = -\beta SI \tag{1a}$$
$$I' = \beta SI - \gamma I \tag{1b}$$
$$R' = \gamma I \tag{1c}$$



Reduction of the model

3 compartments, but when considered in detail, we notice that *removed* do not have a direct influence on the dynamics of S or I, in the sense that R does not appear in (**??**) or (**??**)

Furthermore, the total population (including deceased who are also in R) $N = S + I + R$ satisfies

$$N' = (S + I + R)' = 0$$

Thus, N is constant and the dynamics of R can be deduced from $R = N - (S + I)$

So we now consider

$$S' = -\beta SI \tag{2a}$$
$$I' = \beta SI - \gamma I \tag{2b}$$

Equilibria

Let us consider the equilibria of

$$S' = -\beta SI \qquad \textbf{(??)}$$
$$I' = (\beta S - \gamma)I \qquad \textbf{(??)}$$

From (**??**)

- either $\bar{S} = \gamma/\beta$
- or $\bar{I} = 0$

Substitute into (**??**)

- in the first case, $(\bar{S}, \bar{I}) = (\gamma/\beta, 0)$
- in the second case, any $\bar{S} \geq 0$ is an EP

The second case is an *issue*: the usual linearisation does not work when there is a *continuum* of equilibria as the EP are not *isolated*

Another approach – Study dI/dS

$$S' = -\beta SI \qquad (\textbf{??})$$

$$I' = \beta SI - \gamma I \qquad (\textbf{??})$$

What is the dynamics of dI/dS?

$$\frac{dI}{dS} = \frac{dI}{dt}\frac{dt}{dS} = \frac{I'}{S'} = \frac{\beta SI - \gamma I}{-\beta SI} = \frac{\gamma}{\beta S} - 1 \qquad (4)$$

provided $S \neq 0$

Note – Recall that S and I are $S(t)$ and $I(t)$.. (**??**) thus describes the relation between S and I over solutions to the original ODE (**??**)

Integrate (**??**) and obtain trajectories in state space

$$I(S) = \frac{\gamma}{\beta} \ln S - S + C$$

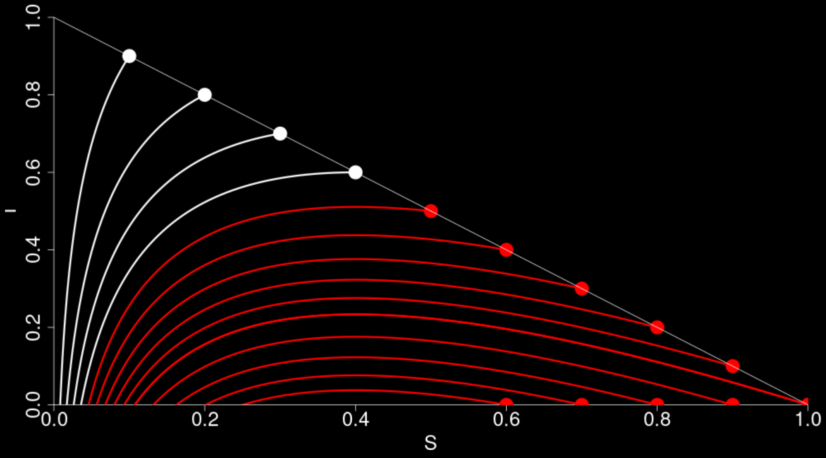
with $C \in \mathbb{R}$

IC $I(S_0) = I_0 \Rightarrow C = S_0 + I_0 - \frac{\gamma}{\beta} \ln S_0$ and the solution to (**??**) is, as a function of S

$$I(S) = S_0 + I_0 - S + \frac{\gamma}{\beta} \ln \frac{S}{S_0}$$
$$R(S) = N - S - I(S) = R_0 - \frac{\gamma}{\beta} \ln \frac{S}{S_0}$$

(since $N_0 = S_0 + I_0 + R_0$)

Trajectories of (**??**) in (S, I)-space, normalised, with IC $(S_0, 1 - S_0)$ and $\beta/\gamma = 2.5$



Let us study

$$I(S) = S_0 + I_0 - S + \frac{\gamma}{\beta} \ln \frac{S}{S_0}$$

We have

$$\frac{d}{dS} I(S) = \frac{\gamma}{\beta S} - 1$$

So, in the previous curves, the max of $I(S)$ happens when $S = \gamma/\beta$ ($S = 0.4$ in the example)

At that point,

$$I(S) = I_0 + \left(1 - \frac{1}{\mathcal{R}_0} - \frac{\ln(\mathcal{R}_0)}{\mathcal{R}_0}\right) S_0$$

Theorem 1 (Epidemic or no epidemic?)

Let $(S(t), I(t))$ *be a solution to* (**??**) *and* $\mathcal{R}_0$ *defined by*

$$\mathcal{R}_0 = \frac{\beta}{\gamma} S_0 \tag{5}$$

- *If* $\mathcal{R}_0 \leq 1$, *then* $I(t) \searrow 0$ *when* $t \to \infty$
- *If* $\mathcal{R}_0 > 1$, *then* $I(t)$ *first reaches a maximum*

$$I_0 + \left(1 - \frac{1}{\mathcal{R}_0} - \frac{\ln(\mathcal{R}_0)}{\mathcal{R}_0}\right) S_0 \tag{6}$$

then goes to 0 as $t \to \infty$

```r
rhs_SIR_KMK <- function(t, x, p) {
  with(as.list(c(x, p)), {
    dS = - beta * S * I
    dI = beta * S * I - gamma * I
    dR = gamma * I
    return(list(c(dS, dI, dR)))
  })
}
# Condition initiale pour S (pour calculer R_0)
S0 = 1000
gamma = 1/14
# Set beta so that R_0 = 1.5
beta = 1.5 * gamma / S0
params = list(gamma = gamma, beta = beta)
IC = c(S = S0, I = 1, R = 0)
times = seq(0, 365, 1)
sol <- ode(IC, times, rhs_SIR_KMK, params)
```

```r
plot(sol[, "time"], sol[, "I"], type = "l",
main = TeX("Kermack-McKendrick SIR, $R_0=1.5$"),
xlab = "Time (days)", ylab = "Prevalence")
```

Final size of an epidemic

For a nonnegative valued integrable function $w(t)$, denote

$$w_\infty = \lim_{t\to\infty} w(t), \qquad \hat{w} = \int_0^\infty w(t)\ dt$$

Denote $w_0 = w(0)$. In the subsystem

$$S' = -\beta S I \qquad \textbf{(??)}$$
$$I' = \beta S I - \gamma I \qquad \textbf{(??)}$$

compute the sum of (**??**) and (**??**), making sure to show time dependence

$$\frac{d}{dt}(S(t) + I(t)) = -\gamma I(t)$$

Integrate from 0 to ∞:

$$\int_0^\infty \frac{d}{dt}(S(t)+I(t))\ dt = -\int_0^\infty \gamma I(t)dt$$

The left hand side gives

$$\int_0^\infty \frac{d}{dt}(S(t)+I(t))\ dt = S_\infty + I_\infty - S_0 - I_0 = S_\infty - S_0 - I_0$$

since $I_\infty = 0$

The right hand side takes the form

$$-\int_0^\infty \gamma I(t)dt = -\gamma \int_0^\infty I(t)dt = -\gamma \hat{I}$$

We thus have

$$S_\infty - S_0 - I_0 = -\gamma \hat{I} \tag{7}$$

Now consider (**??**):

$$S' = -\beta S I$$

Divide both sides by S:

$$\frac{S'(t)}{S(t)} = -\beta I(t)$$

Integrate from 0 to ∞:

$$\ln S_\infty - \ln S_0 = -\beta \hat{I} \tag{8}$$

Express (**??**) and (**??**) in terms of $-\hat{I}$ and equate

$$\frac{\ln S_\infty - \ln S_0}{\beta} = \frac{S_\infty - S_0 - I_0}{\gamma}$$

Thus we have

$$(\ln S_0 - \ln S_\infty) S_0 = (S_0 - S_\infty)\mathcal{R}_0 + I_0 \mathcal{R}_0 \tag{9}$$

Theorem 2 (Final size relation)

Let $(S(t), I(t))$ be a solution to (**??**) *and $\mathcal{R}_0$ defined by* (**??**)

The number $S(t)$ of susceptible individuals is a nonincreasing function and its limit S_∞ is the only solution in $(0, S_0)$ of the transcendental equation

$$(\ln S_0 - \ln S_\infty) S_0 = (S_0 - S_\infty)\mathcal{R}_0 + I_0 \mathcal{R}_0 \qquad \textbf{(??)}$$

The (transcendantal) final size equation

Rewrite the final size equation

$$(\ln S_0 - \ln S_\infty)S_0 = (S_0 - S_\infty)\mathcal{R}_0 + I_0\mathcal{R}_0 \qquad \textbf{(??)}$$

as

$$T(S_\infty) = (\ln S_0 - \ln S_\infty)S_0 - (S_0 - S_\infty)\mathcal{R}_0 - I_0\mathcal{R}_0 \qquad (10)$$

Thus, we seek the zeros of the function $T(S_\infty)$

We seek S_∞ in $(0, S_0]$ s.t. $T(S_\infty) = 0$, with

$$T(S_\infty) = (\ln S_0 - \ln S_\infty)S_0 - (S_0 - S_\infty)\mathcal{R}_0 - I_0\mathcal{R}_0 \qquad \textbf{(??)}$$

Note to begin that

$$\lim_{S_\infty \to 0} T(S_\infty) = \lim_{S_\infty \to 0} -S_0 \ln(S_\infty) = \infty$$

Differentiating T with respect to S_∞, we get

$$T'(S_\infty) = \mathcal{R}_0 - S_0/S_\infty$$

When $S_\infty \to 0$, $\mathcal{R}_0 - S_0/S_\infty < 0$, so T decreases to $S_\infty = S_0/\mathcal{R}_0$

So if $\mathcal{R}_0 \leq 1$, the function T is decreasing on $(0, S_0)$, while it has a minimum if $\mathcal{R}_0 > 1$

Case $\mathcal{R}_0 \leq 1$

$$T(S_\infty) = (\ln S_0 - \ln S_\infty)S_0 - (S_0 - S_\infty)\mathcal{R}_0 - I_0\mathcal{R}_0 \qquad \textbf{(??)}$$

- We have seen that T decreases on $(0, S_0]$
- Also, $T(S_0) = -I_0\mathcal{R}_0 < 0$ ($I_0 = 0$ is trivial and not considered)
- T is continuous

$\implies$ there exists a unique $S_\infty \in (0, S_0]$ s.t. $T(S_\infty) = 0$

Case $\mathcal{R}_0 > 1$

$$T(S_\infty) = (\ln S_0 - \ln S_\infty)S_0 - (S_0 - S_\infty)\mathcal{R}_0 - I_0\mathcal{R}_0 \qquad \textbf{(??)}$$

- We have seen that T decreases on $(0, S_0/\mathcal{R}_0]$
- For $S_\infty \in [S_0/\mathcal{R}_0]$, $T' > 0$
- As before, $T(S_\infty) = -I_0\mathcal{R}_0$
- T is continuous

$\implies$ there exists a unique $S_\infty \in (0, S_0]$ s.t. $T(S_\infty) = 0$. More precisely, in this case, $S_\infty \in (0, S_0/\mathcal{R}_0)$

We solve numerically. We need a function

```
final_size_eq = function(S_inf, S0 = 999, I0 = 1, R_0 = 2.5) {
  OUT = S0*(log(S0)-log(S_inf)) - (S0+I0-S_inf)*R_0
  return(OUT)
}
```

and solve easily using `uniroot`, here with the values by default that we have set for the function

```
uniroot(f = final_size_eq, interval = c(0.05, 999))
$root
[1] 106.8819
$f.root
[1] -2.649285e-07
$iter
[1] 10
$init.it
[1] NA
$estim.prec
[1] 6.103516e-05
```

To use something else than the default values, e.g.,

```
N0 = 1000
I0 = 1
S0 = N0-I0
R_0 = 2.4
uniroot(
  f = function(x)
    final_size_eq(S_inf = x,
                  S0 = S0, I0 = I0,
                  R_0 = R_0),
  interval = c(0.05, S0))
```

A figure with all the information

```
S = seq(0.1, S0, by = 0.1)
fs = final_size(S, S0 = S0, I0 = I0, R_0 = R_0)
S_inf = uniroot(f = function(x) final_size_eq(S_inf = x,
                                              S0 = S0, I0 = I0,
                                              R_0 = R_0),
                interval = c(0.05, S0))
plot(S, fs, type = "l", ylab = "Value␣of␣equation␣(10)")
abline(h = 0)
points(x = S_inf$root, y = 0, pch = 19)
text(x = S_inf$root, y = 0, labels = "S_inf", adj = c(-0.25,-1))
```

$\mathcal{R}_0 = 0.8$

$\mathcal{R}_0 = 2.4$

A little nicer

```
values = expand.grid(
  R_0 = seq(0.01, 3, by = 0.01),
  I0 = 1:100
)
values$S0 = N0-values$I0
L = split(values, 1:nrow(values))

values$S_inf = sapply(X = L, FUN = final_size)

values$taille_finale = values$S0-values$S_inf+values$I0
values$taux_attaque = (values$taille_finale / N0)*100

levelplot(taux_attaque ~ R_0*I0, data = values,
          xlab="R_0", ylab = "I0",
          col.regions = viridis(100))
```

(requires `lattice` and `viridis` librairies)

Attack rate (in %)

The simplest vaccination model

To implement vaccination in KMK, assume that vaccination reduces the number of susceptibles

Let total population be N with S_0 initially susceptible

Vaccinate a fraction $p \in [0, 1]$ of susceptible individuals

Original IC (for simplicity, $R(0) = 0$)

$$IC : (S(0), I(0), R(0)) = (S_0, I_0, 0) \tag{11}$$

Post-vaccination IC

$$IC : (S(0), I(0), R(0)) = ((1 - p)S_0, I_0, pS_0) \tag{12}$$

Vaccination reproduction number

Without vaccination

$$\mathcal{R}_0 = \frac{\beta}{\gamma} S_0 \qquad \textbf{(??)}$$

With vaccination, denoting $\mathcal{R}_0^{\mathsf{v}}$ the reproduction number,

$$\mathcal{R}_0^{\mathsf{v}} = \frac{\beta}{\gamma}(1-p)S_0 \qquad (13)$$

Since $p \in [0,1]$, $\mathcal{R}_0^{\mathsf{v}} \leq \mathcal{R}_0$

Herd immunity

Therefore

- $\mathcal{R}_0^{\mathrm{v}} < \mathcal{R}_0$ if $p > 0$
- To control the disease, $\mathcal{R}_0^{\mathrm{v}}$ must take a value less than 1

To make $\mathcal{R}_0^{\mathrm{v}}$ less than 1

$$\mathcal{R}_0^{\mathrm{v}} < 1 \iff p > 1 - \frac{1}{\mathcal{R}_0} \tag{14}$$

By vaccinating a fraction $p > 1 - 1/\mathcal{R}_0$ of the susceptible population, we thus are in a situation where an epidemic peak is precluded (or, at the very least, the final size is reduced)

This is **herd immunity**

An SIR model with vaccination

Take SIR model and assume the following

- Vaccination takes susceptible individuals and moves them directly into the recovered compartment, without them ever becoming infected/infectious

- Birth = death

- A fraction p is vaccinated at birth

- $f(S, I, N) = \beta SI$

$$S' = (1 - p)dN - dS - \beta SI \tag{15a}$$
$$I' = \beta SI - (d + \gamma)I \tag{15b}$$
$$R' = pdN + \gamma I - dR \tag{15c}$$

Computation of $\mathcal{R}_0$

- DFE, SIR:

$$E_0 := (S, I, R) = (N, 0, 0)$$

- DFE, SIR with vaccination

$$E_0^v := (S, I, R) = ((1-p)N, 0, pN)$$

Thus, - In SIR case

$$\mathcal{R}_0 = \frac{\beta N}{d + \gamma}$$

- In SIR with vaccination case, denote $\mathcal{R}_0^v$ and

$$\mathcal{R}_0^v = (1-p)\mathcal{R}_0$$

Herd immunity

Therefore - $\mathcal{R}_0^{\mathrm{v}} < \mathcal{R}_0$ if $p > 0$ - To control the disease, $\mathcal{R}_0^{\mathrm{v}}$ must take a value less than 1, i.e.,

$$\mathcal{R}_0^{\mathrm{v}} < 1 \iff p > 1 - \frac{1}{\mathcal{R}_0} \tag{16}$$

By vaccinating a fraction $p > 1 - 1/\mathcal{R}_0$ of newborns, we thus are in a situation where the disease is eventually eradicated

This is **herd immunity**

To normalise or not to normalise?

- In the SIS of Lecture 05 and here, since the total population is constant, it is possible to normalise to $N = 1$
- This can greatly simplify some computations
- However, I am not a big fan: it is important to always have the "sizes" of objects in mind
- If you do normalise, at least for a paper destined to mathematical biology, always do a "return to biology", i.e., interpret your results in a biological light, which often implies to return to original values

Where we are

- An *endemic* SIS model in which the threshold $\mathcal{R}_0 = 1$ is such that, when $\mathcal{R}_0 < 1$, the disease goes extinct, whereas when $\mathcal{R}_0 > 1$, the disease becomes established in the population

- An *epidemic* SIR model (the KMK SIR) in which the presence or absence of an epidemic wave is characterised by the value of $\mathcal{R}_0$

- The SIS and the KMK SIR have explicit solutions (in some sense). **This is an exception!**