The Kermack-McKendrick model

MATH 8xyz – Lecture 04

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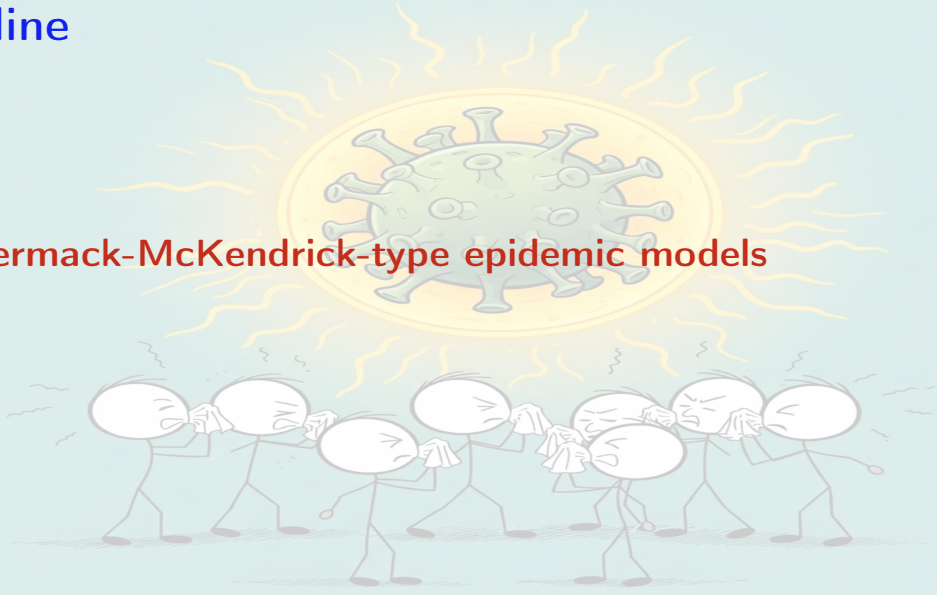
The University of Manitoba campuses are located on original lands of Anishinaabeg, Ininew, Anisininew, Dakota and Dene peoples, and on the National Homeland of the Red River Métis.
We respect the Treaties that were made on these territories, we acknowledge the harms and mistakes of the past, and we dedicate ourselves to move forward in partnership with Indigenous communities in a spirit of Reconciliation and collaboration.

Outline

Kermack-McKendrick-type epidemic models



Kermack and McKendrick (1927+)

Model in these slides 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)

Kermack-McKendrick-type epidemic models

A Contribution to the Mathematical Theory of Epidemics.

By W. O. KERMACK and A. G. MCKENDRICK.

(Communicated by Sir Gilbert Walker, F.R.S.—Received May 13, 1927.)

(From the Laboratory of the Royal College of Physicians, Edinburgh.)

Introduction.

(1) One of the most striking features in the study of epidemics is the difficulty of finding a causal factor which appears to be adequate to account for the magnitude of the frequent epidemics of disease which visit almost every population. It was with a view to obtaining more insight regarding the effects of the various factors which govern the spread of contagious epidemics that the present investigation was undertaken. Reference may here be made to the work of Ross and Hudson (1915–17) in which the same problem is attacked. The problem is here carried to a further stage, and it is considered from a point of view which is in one sense more general. The problem may be summarised as follows: One (or more) infected person is introduced into a community of individuals, more or less susceptible to the disease in question. The disease spreads from

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?

Kermack-McKendrick-type epidemic models

- The Kermack-McKendrick (KMK) model
- Mathematical analysis of KMK
- The final size of a KMK epidemic
- Herd immunity in KMK

In this case the equations are

$$\left.\begin{aligned} \frac{dx}{dt} &= -\kappa xy \\ \frac{dy}{dt} &= \kappa xy - ly \\ \frac{dz}{dt} &= ly \end{aligned}\right\}$$

and as before $x + y + z = \mathrm{N}$.

The Kermack-McKendrick 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*)

- Individuals are either *susceptible* to the disease or *infected* by (and *infectious* with) the disease

- After recovering or dying from the disease, individuals are *removed* from the infectious compartment (R)

- Incidence is of **mass action** type and takes the form βSI

The state variables

We formulate the model as a system of **differential equations**

Differential equations: unknowns are *functions* (instead of scalars, like in algebraic equations)

At time $t \geq 0$ (we typically assume time starts at $t = 0$, but could also consider $t \geq t_0 > 0$), the **state variables**, in the current model, are the numbers of individuals who are

- susceptible to the disease: $S(t)$
- infected and infectious with the disease: $I(t)$
- removed from the infectious comparment: $R(t)$

Often, we drop the dependence on t if it is not explicitly required and write S, I, R

Important – Incidence functions

Incidence is the rate at which new cases arise, the incidence function then describes how contacts lead to new infections

If there are S susceptible individuals and I infectious individuals in the population, we use a function of the form

$$f(S, I)$$

The function can also explicitly depend on the total population N, i.e., $f(S, I, N)$

We return to incidence functions in Lecture 06

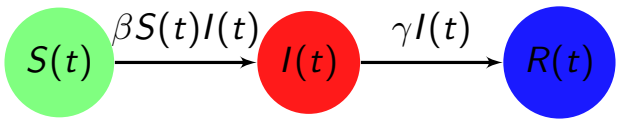
For now, just know the most common incidence functions are

- **mass action incidence** $f(S, I, N) = \beta SI$
- **standard** (or **proportional**) **incidence** $f(S, I, N) = \beta SI/N$

The Kermack-McKendrick model

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

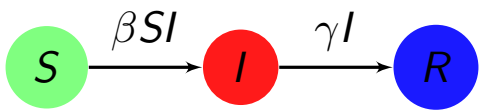
$$\frac{d}{dt}S(t) = -\beta S(t)I(t)$$
$$\frac{d}{dt}I(t) = \beta S(t)I(t) - \gamma I(t)$$
$$\frac{d}{dt}R(t) = \gamma I(t)$$



The Kermack-McKendrick model

As indicated, we often drop dependence on t of the state variables; we also write $X' := dX(t)/dt$. So the KMK model is usually written

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



Kermack-McKendrick-type epidemic models

The Kermack-McKendrick (KMK) model

Mathematical analysis of KMK

The final size of a KMK epidemic

Herd immunity in KMK

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 (1a) or (1b)

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

$$S(t) + I(t) + R(t) = N_0, \quad t \geq 0. \tag{2}$$

so the dynamics of R can be deduced from $R = N - (S + I)$. So we can consider

$$S' = -\beta SI \tag{3a}$$
$$I' = \beta SI - \gamma I \tag{3b}$$

Equilibria

Let us consider the equilibria of

$$S' = -\beta SI \tag{3a}$$
$$I' = (\beta S - \gamma)I \tag{3b}$$

From (3b)

- either $S^\star = \gamma/\beta$
- or $I^\star = 0$

Substitute into (3a)

- in the first case, $(S^\star, I^\star) = (\gamma/\beta, 0)$
- in the second case, any $S^\star \geq 0$ 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*

What is the problem with non-isolated EP?

Proposition 1

The Kermack-McKendrick model SIR model (1) *has the continuum of equilibria*

$$E_0^{KMK} := \{(S^\star, I^\star, R^\star) = (S_\infty, 0, N_0 - S_\infty), \quad S_\infty \in [0, N_0]\} \tag{5}$$

Proof

Let us consider (1) and start with $I = I^\star = 0$. Substitute this value into (1a) at equilibrium, giving $0 = -\gamma S^\star I^\star (= 0)$, meaning that any value of $S^\star$ satisfies this relation. From the conservation of the total population (2), the equilibrium E_0^{KMK} takes the form given by (5)

Now consider $S = S^\star = \gamma/\beta$. Substituting this value into (1a) at equilibrium gives $0 = -\gamma I^\star$, from which it follows that $I^\star = 0$, and, using the conservation of total population (2),

$$(S^\star, I^\star, R^\star) = \left(\frac{\gamma}{\beta}, 0, N_0 - \frac{\gamma}{\beta}\right) \tag{6}$$

is an equilibrium of (1). The equilibrium (6) is biologically relevant only when $N_0 - \gamma/\beta \geq 0$. Note that (5) includes (6) when the latter is biologically relevant

Adapting slightly the definitions in [?], consider the ordinary differential equation

$$x' = f(x) \tag{7}$$

where $x(t) \in W$ and $f : W \to E$ is a function such that solutions to (7) exist uniquely, e.g., a C^1 function, from an open set W of the vector space E into E

Denote $x(t, x_0)$ the solution to (7) through the initial value $x(t_0) = x_0$

A point $x^\star \in W$ is an **equilibrium** if $f(x^\star) = 0$

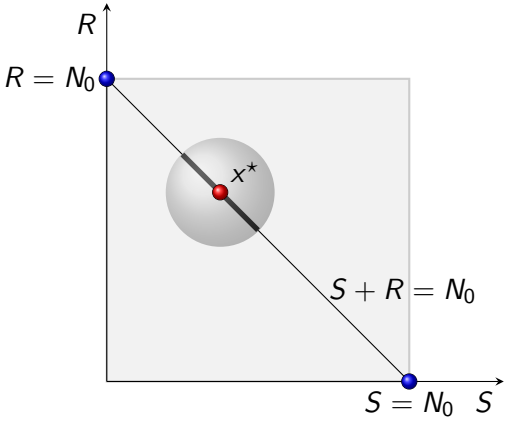
Definition 2 (Locally stable equilibrium)

An equilibrium point $x^\star$ of (7) is **locally stable** (LS) if for every neighbourhood $\mathcal{N}(x^\star)$ of $x^\star$ in W, there is a neighbourhood $\mathcal{N}_1 \subseteq \mathcal{N}(x^\star)$ of $x^\star$ such that every solution $x(t, x_0)$ with $x_0 \in \mathcal{N}_1$ is defined and in $\mathcal{N}(x^\star)$ for all $t > t_0$

Definition 3 (Locally asymptotically stable equilibrium)

If $\mathcal{N}_1$ can be chosen so that in addition to the properties in Definition 2, $\lim_{t\to\infty} x(t, x_0) = x^\star$ for all $x_0 \in \mathcal{N}_1$, then $x^\star$ is **locally asymptotically stable** (LAS)

DFE (5) of (1) are not **isolated**: any (open) neighbourhood of an equilibrium contains infinitely many other equilibria



Neighbourhood $\mathcal{N}(x^\star)$ of $x^\star \in E_0^{\mathrm{KMK}}$ lying on the $S-R$ plane (the neighbourhood extends above and below the $S-R$ plane in the I direction, not shown here). The thin line is E_0^{KMK}, the thick line is $E_0^{\mathrm{KMK}} \cap \mathcal{N}(x^\star)$

Proposition 4

Consider a disease-free equilibrium $x^\star \in E_0^{KMK}$ *of* (1)*. Then* $x^\star$ *is LS but not LAS*

This means in particular that considering the Jacobian of (1) at the DFE **makes no sense**!

Proof

Let $x_1^\star \in E_0^{\text{KMK}}$ be an equilibrium of (1). Consider $\mathcal{S}_\mathcal{N}(x_1^\star) \subset E_0^{\text{KMK}}$, open subset of E_0^{KMK} containing $x_1^\star$. Now take some $x_2^\star \in \mathcal{S}_\mathcal{N}(x_1^\star)$. Since $x_2^\star \in \mathcal{S}_\mathcal{N}(x_1^\star) \subset E_0^{\text{KMK}}$, $x_2^\star$ is an equilibrium of (1) and thus $x(t, x_2^\star) = x_2^\star \in \mathcal{S}_\mathcal{N}(x_1^\star)$ for all $t \geq t_0$. As a consequence, $x_1^\star$ is locally stable

$\Rightarrow$ any open neighbourhood $\mathcal{N}(x_1^\star)$ contains $\mathcal{S}_\mathcal{N} = \mathcal{N}(x_1^\star) \cap E_0^{\text{KMK}}$

Consider, then, some $x_2^\star \in \mathcal{S}_\mathcal{N}$. Since $x_2^\star \in \mathcal{S}_\mathcal{N}$, $x_2^\star$ is an equilibrium and as a consequence, $\lim_{t\to\infty} x(t, x_2^\star) = x_2^\star$. Therefore, any open neighbourhood of $x_1^\star$ contains points x_0 not such that $\lim_{t\to\infty} x(t, x_0) = x_1^\star \implies x_1^\star$ is LS but not LAS

The next generation matrix method in this context

Consider the method in [**?**]

To construct $\mathcal{R}_0$, they require *local stability*

Theorem 2 in [**?**] pertaining to LAS, on the other hand, has one assumption (assumption A5) that the DFE be *locally asymptotically stable*, with the assumption that all eigenvalues of the linearisation near a disease-free equilibrium have negative real parts

Clearly, this cannot be true with (1)

Another approach – Study dI/dS

$$S' = -\beta SI \tag{3a}$$
$$I' = \beta SI - \gamma I \tag{3b}$$

What is the dynamics of dI/dS?

$$\frac{dI}{dS} = \frac{dI}{dt}\frac{dt}{dS} = \frac{I'}{S'} = \frac{\beta SI - \gamma I}{-\beta SI} = \frac{\gamma}{\beta S} - 1 \tag{8}$$

provided $S \neq 0$

Note – Recall that S and I are $S(t)$ and $I(t)$.. (8) thus describes the relation between S and I over solutions to the original ODE (3)

Integrate (8) and obtain trajectories in state space

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

with $C \in \mathbb{R}$

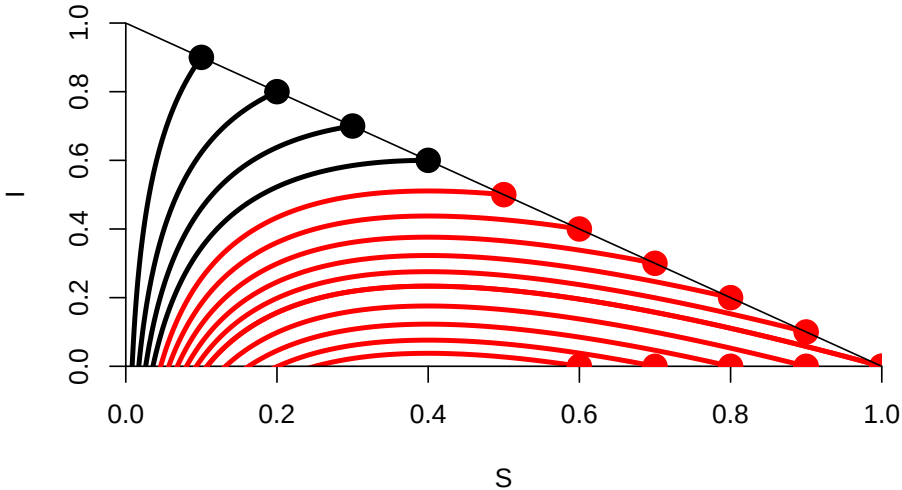
IC $I(S_0) = I_0 \Rightarrow C = S_0 + I_0 - \frac{\gamma}{\beta} \ln S_0$ and the solution to (1) is, as a function of S

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

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

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

Trajectories of (3) 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 5 (Epidemic or no epidemic?)

Let $(S(t), I(t))$ be a solution to (3) and $\mathcal{R}_0$ defined by

$$\mathcal{R}_0 = \frac{\beta}{\gamma} S_0 \tag{9}$$

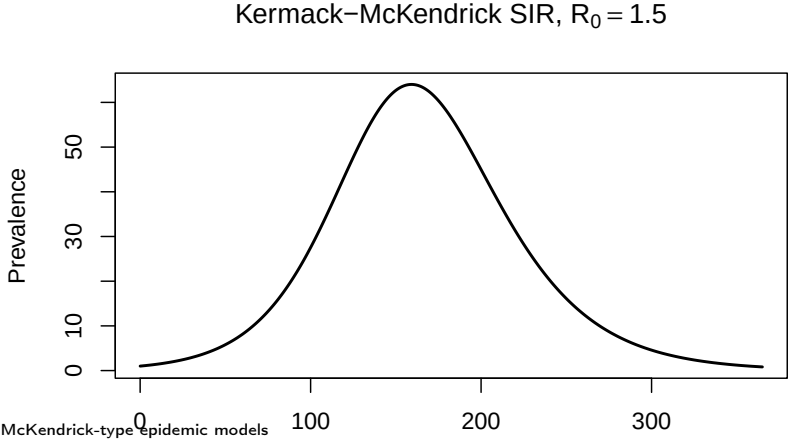
- *If $\mathcal{R}_0 \leq 1$, then $I(t) \searrow 0$ when $t \to \infty$*
- *If $\mathcal{R}_0 > 1$, then $I(t)$ first reaches a maximum*

$$I_0 + \left(1 - \frac{1}{\mathcal{R}_0} - \frac{\ln(\mathcal{R}_0)}{\mathcal{R}_0}\right) S_0 \tag{10}$$

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)))
  })
}
# Initial condition for S (to compute 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_KMK <- ode(IC, times, rhs_SIR_KMK, params)
```

```r
plot(sol_KMK[, "time"], sol_KMK[, "I"],
     type = "l", lwd = 2,
     main = TeX("Kermack-McKendrick SIR, $R_0=1.5$"),
     xlab = "Time (days)", ylab = "Prevalence")
```



The basic reproduction number $\mathcal{R}_0$

- Indicator often used in epidemiology. Verbally
  average number of secondary cases of infection produced when a single infectious individual is introduced in a wholly susceptible population

- If $\mathcal{R}_0 < 1$, then each infectious individual infects on average less than 1 person and the epidemic is quite likely to go extinct

- If $R_0 > 1$, then each infectious individual infects on average more than 1 person and an epidemic is quite likely to occur

A few sample values of $\mathcal{R}_0$

$\mathcal{R}_0$ can be estimated from data (from the Anderson & May book)

Infection	Location	Period	$\mathcal{R}_0$
Measles	Cirencester, England	1947-50	13-14
	England and Wales	1950-68	16-18
	Kansas, USA	1918-21	5-6
	Ontario, Canada	1912-3	11-12
	Willesden, England	1912-3	11-12
	Ghana	1960-8	14-15
	East Nigeria	1960-8	16-17

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Final size of an epidemic

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

$$w_0 = w(0), \qquad w_\infty = \lim_{t\to\infty} w(t), \qquad \hat{w} = \int_0^\infty w(t)\ dt$$

In the subsystem

$$S' = -\beta SI \tag{3a}$$
$$I' = \beta SI - \gamma I \tag{3b}$$

compute the sum of (3a) and (3b), 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

$$S_\infty - S_0 - I_0 = -\gamma \hat{I} \tag{11}$$

Now consider (3a):

$$S' = -\beta SI$$

Divide both sides by S:

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

Integrate from 0 to ∞:

$$\ln S_\infty - \ln S_0 = -\beta \hat{I} \tag{12}$$

Express (11) and (12) 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

$$(\ln S_0 - \ln S_\infty)S_0 = (S_0 - S_\infty)\mathcal{R}_0 + I_0\mathcal{R}_0 \tag{13}$$

Theorem 6 (Final size relation)

Let $(S(t), I(t))$ *be a solution to* (3) *and* $\mathcal{R}_0$ *defined by* (9)

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*

$$(\ln S_0 - \ln S_\infty)S_0 = (S_0 - S_\infty)\mathcal{R}_0 + I_0\mathcal{R}_0 \tag{13}$$

The (transcendantal) final size equation

Rewrite the final size equation

$$(\ln S_0 - \ln S_\infty)S_0 = (S_0 - S_\infty)\mathcal{R}_0 + I_0\mathcal{R}_0 \tag{13}$$

as

$$T(S_\infty) = (\ln S_0 - \ln S_\infty)S_0 - (S_0 - S_\infty)\mathcal{R}_0 - I_0\mathcal{R}_0 \tag{14}$$

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

$$T(S_\infty) = (\ln S_0 - \ln S_\infty)S_0 - (S_0 - S_\infty)\mathcal{R}_0 - I_0\mathcal{R}_0 \tag{14}$$

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 $\mathcal{R}_0 \leq 1$

$$T(S_\infty) = (\ln S_0 - \ln S_\infty)S_0 - (S_0 - S_\infty)\mathcal{R}_0 - I_0\mathcal{R}_0 \tag{14}$$

- 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

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

Case $\mathcal{R}_0 > 1$

$$T(S_\infty) = (\ln S_0 - \ln S_\infty)S_0 - (S_0 - S_\infty)\mathcal{R}_0 - I_0\mathcal{R}_0 \tag{14}$$

- 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

$\Longrightarrow$ 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`:

```
uniroot(f = final_size_eq, interval = c(0.05, 999))
```

```
## $root
## [1] 106.8819
##
## $f.root
## [1] -2.649285e-07
##
## $iter
## [1] 10
##
```

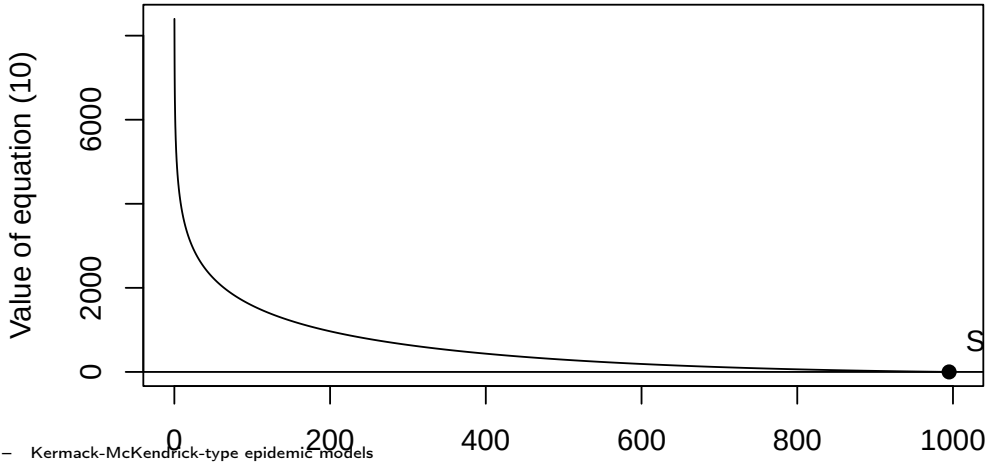
A function to use this..

```
final_size = function(L) {
  with(as.list(L), {
  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))
  return(S_inf$root)
  })
}
```

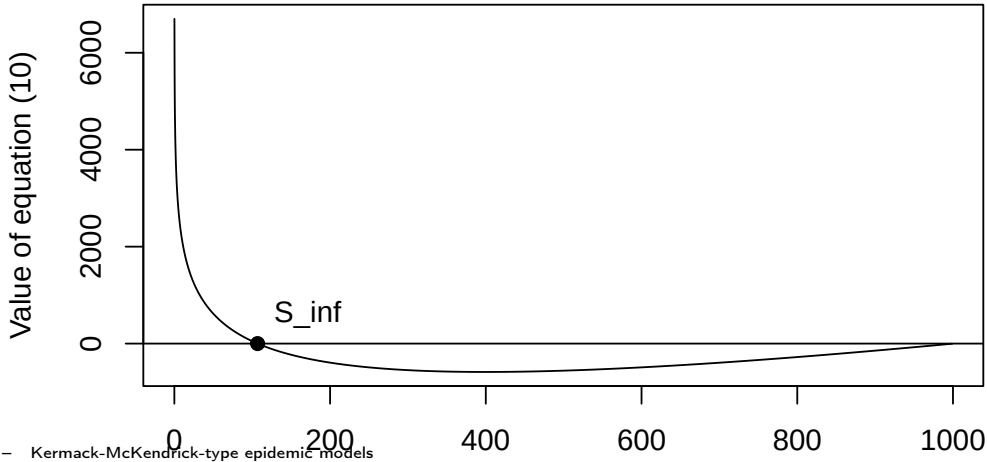
A figure with all the information

```
N0 = 1000
I0 = 1
S0 = N0-I0
R_0 = 0.8
S = seq(0.1, S0, by = 0.1)
fs = final_size_eq(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))
```

$\mathcal{R}_0 = 0.8$



$\mathcal{R}_0 = 2.4$



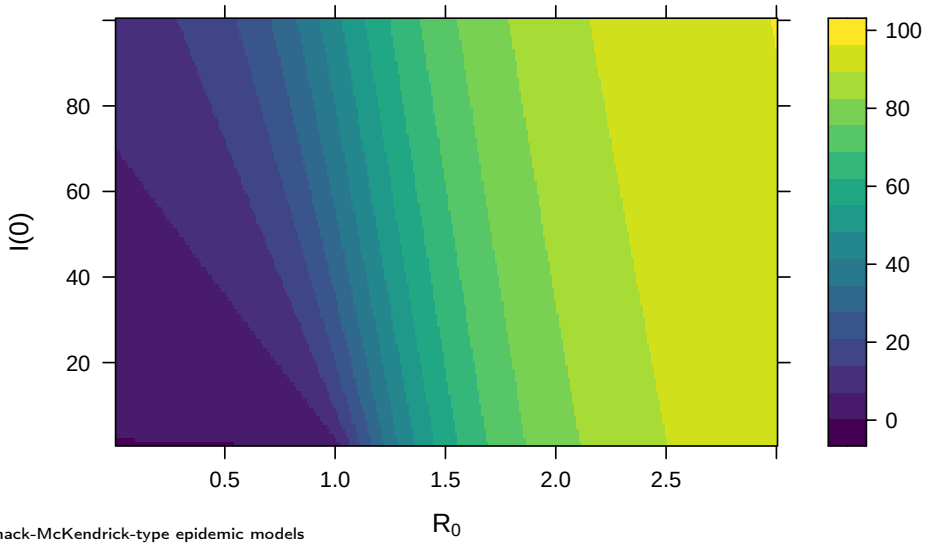
A little nicer

```
values = expand.grid(
  R_0 = seq(0.01, 3, by = 0.01),
  I0 = seq(1, 100, 1)
)
values$S0 = N0-values$I0
L = split(values, 1:nrow(values))
values$S_inf = sapply(X = L, FUN = final_size)
values$final_size = values$S0-values$S_inf+values$I0
values$attack_rate = (values$final_size / N0)*100

p = levelplot(attack_rate ~ R_0*I0, data = values,
              xlab = TeX("$R_0$"), ylab = "I(0)",
              col.regions = viridis(100))
print(p)
```

(requires `lattice`, `viridis` and `latex2exp` librairies)

Attack rate (in %)



Kermack-McKendrick-type epidemic models

- The Kermack-McKendrick (KMK) model
- Mathematical analysis of KMK
- The final size of a KMK epidemic
- **Herd immunity in KMK**

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, $R(0) = 0$)

$$IC : (S(0), I(0), R(0)) = (S_0, I_0, 0) \tag{15}$$

Post-vaccination IC

$$IC : (S(0), I(0), R(0)) = ((1 - p)S_0, I_0, pS_0) \tag{16}$$

Vaccination reproduction number

Without vaccination

$$\mathcal{R}_0 = \frac{\beta}{\gamma} S_0 \tag{9}$$

With vaccination, denoting $\mathcal{R}_v$ the reproduction number,

$$\mathcal{R}_v = \frac{\beta}{\gamma}(1-p)S_0 \tag{17}$$

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

Herd immunity

Therefore

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

To make $\mathcal{R}_v$ less than 1

$$\mathcal{R}_v < 1 \iff p > 1 - \frac{1}{\mathcal{R}_0} \tag{18}$$

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**

Bibliography I