Infectious disease epidemiology & Mathematical modeling

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# Program

<table>
<thead>
<tr>
<th>Lesson 1</th>
<th>SARS 2002/2003: why modeling, and what is a mathematical model? (the example of bacterial growth)</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exercise 1</td>
<td>Design a mathematical model yourself: the bacterial growth curve (iterative solution of the bacterial growth curve with Excel)</td>
<td>11</td>
</tr>
<tr>
<td>Exercise 2</td>
<td>Solve the bacterial growth with Runge-Kutta software</td>
<td>17</td>
</tr>
<tr>
<td>Lesson 2</td>
<td><strong>Deterministic models</strong>: SIR-model, theory, basic reproduction number $R_0$, epidemic vs. endemic case</td>
<td>19</td>
</tr>
<tr>
<td>Exercise 3</td>
<td>Simulate: epidemic according to the SIR model</td>
<td>29</td>
</tr>
<tr>
<td>Exercise 4</td>
<td>Think longterm: the influence of time and demography (The example of measles as an endemic infection)</td>
<td>38</td>
</tr>
<tr>
<td>Lesson 3</td>
<td><strong>Vaccination</strong>: final size of an epidemic, critical vaccination coverage</td>
<td>41</td>
</tr>
<tr>
<td>Exercise 5</td>
<td>Predict: how many newborns to vaccinate? (sensitivity analyses into the critical vaccination coverage)</td>
<td>44</td>
</tr>
<tr>
<td>AddOn</td>
<td>InfluSim</td>
<td>56</td>
</tr>
</tbody>
</table>
Literature selection

- Mathematical Epidemiology of Infectious Diseases: Model Building, Analysis and Interpretation (Wiley Series in Mathematical and Computational Biology), O. Diekmann and J. A. P. Heesterbeek.
- Epidemic Models: Their Structure and Relation to Data (Publications of the Newton Institute). Denis Mollison
Lesson 1

SARS 2002/2003:
why modeling, and what is a mathematical model?
(the example of bacterial growth)
Example SARS 2003/2004

<table>
<thead>
<tr>
<th>Country</th>
<th>Cases</th>
<th>Deaths</th>
<th>Case fatality [%]</th>
</tr>
</thead>
<tbody>
<tr>
<td>China</td>
<td>5327</td>
<td>349</td>
<td>7</td>
</tr>
<tr>
<td>Hong Kong</td>
<td>1755</td>
<td>296</td>
<td>17</td>
</tr>
<tr>
<td>Taiwan</td>
<td>665</td>
<td>180</td>
<td>27</td>
</tr>
<tr>
<td>Kanada</td>
<td>251</td>
<td>41</td>
<td>16</td>
</tr>
<tr>
<td>Singapur</td>
<td>238</td>
<td>33</td>
<td>14</td>
</tr>
<tr>
<td>Vietnam</td>
<td>63</td>
<td>5</td>
<td>8</td>
</tr>
<tr>
<td>USA</td>
<td>33</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Philippinen</td>
<td>14</td>
<td>2</td>
<td>14</td>
</tr>
<tr>
<td>Deutschland</td>
<td>9</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

8355 906 10.8%

For comparison Malaria: ~300 Mio. Cases / Year, 
~1 Mio Deaths / Year (predominantly children)
On 21 February, a Chinese doctor who had treated as yet undiagnosed SARS patients in Guangdong Province checked into the Metropole Hotel in Hong Kong. Within twenty-four hours, 12 people who stayed in the same hotel became infected with SARS and took the disease with them to Singapore, Hong Kong, Vietnam, Ireland, Canada, and the United States, infecting directly or indirectly more than 350 people. Eventually, the World Health Organization estimated that more than 4,000 cases worldwide could be traced to this "superspreader".
Spread from Hotel Metropole

Spread from Hotel M
Reported as of March 28, 2003

Key:
- Basic reproduction number

Hans-Peter Duerr, University of Tuebingen, www.uni-tuebingen.de/modeling
Problem Global Networks

e.g. between Chicago and New York 25,000 Passengers per day

L. Hufnagel et al. 2004, PNAS 101: 15124-9

Key words: Model, Networks
Prediction

Fig. 2. Global spread of SARS. (A) Geographical representation of the global spreading of probable SARS cases on May 30, 2003, as reported by the WHO and Centers for Disease Control and Prevention. The first cases of SARS emerged in mid-November 2002 in Guangdong Province, China (17). The disease was then carried to Hong Kong on the February 21, 2003, and began spreading around the world along international air travel routes, because tourists and the medical doctors who treated the early cases traveled internationally. As the disease moved out of southern China, the first hot zones of SARS were Hong Kong, Singapore, Hanoi (Vietnam), and Toronto (Canada), but soon cases in Taiwan, Thailand, the U.S., Europe, and elsewhere were reported. (B) Geographical representation of the results of our simulations 90 days after an initial infection in Hong Kong. The simulation corresponds to the real SARS infection at the end of May 2003. Because our simulations cannot describe the infection in China, where the disease started in November 2002, we used the WHO data for China.

L. Hufnagel et al. 2004, PNAS 101: 15124-9
What is a mathematical Model?

Example bacterial growth: bacteria divide 2 times per hour.

→ **Duration** between divisions \( D = 0.5 \) hours.
→ **Rate** of division \( \lambda = \frac{1}{D} \)

Growth from one generation to the next:

Model:

\[
B_i = 2B_{i-1}
\]

\[
B(t) = B_0 \cdot 2^{\lambda t}
\]

Problems of this approach:
- only valid for initial growth
- too simple for describing complex processes
Exercise 1: preliminary considerations

Draw into each graph the bacterial growth curve you would expect if

• ... the culture was started with 10000 bacteria, rather than 1 bacteria

• ... the generation time of the bacterium was not 0.5h but 1h

• ... the before-mentioned changes occur simultaneously
Exercise 1: iterative solution of the model in Excel

Complete cells B2 to C32 in file "00_Bakterienwachstum.xls", spreadsheet "generation time"

1. Parameter: "Bakt0"
2. Parameter: "tGen"
3. Parameter: "multFaktor"

\[ =A2 \times tGen \]
\[ =Bakt0 \]
\[ =A2 \times tGen \]
\[ =C2 \times \text{multFaktor} \]
Exercise 1 (File "00_bacterialGrowth.xls", sheet "generation time")

Verify the preliminary considerations of the previous slide.

<table>
<thead>
<tr>
<th>Generation</th>
<th>Time [hours]</th>
<th>No. of bacteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>3</td>
<td>0.5</td>
<td>2</td>
</tr>
<tr>
<td>4</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>5</td>
<td>1.5</td>
<td>8</td>
</tr>
<tr>
<td>6</td>
<td>2</td>
<td>16</td>
</tr>
<tr>
<td>7</td>
<td>2.5</td>
<td>32</td>
</tr>
<tr>
<td>8</td>
<td>3</td>
<td>64</td>
</tr>
<tr>
<td>9</td>
<td>3.5</td>
<td>128</td>
</tr>
<tr>
<td>10</td>
<td>4</td>
<td>256</td>
</tr>
<tr>
<td>11</td>
<td>4.5</td>
<td>512</td>
</tr>
<tr>
<td>12</td>
<td>5</td>
<td>1024</td>
</tr>
<tr>
<td>13</td>
<td>5.5</td>
<td>2048</td>
</tr>
<tr>
<td>14</td>
<td>6</td>
<td>4096</td>
</tr>
<tr>
<td>15</td>
<td>6.5</td>
<td>8192</td>
</tr>
<tr>
<td>16</td>
<td>7</td>
<td>16384</td>
</tr>
<tr>
<td>17</td>
<td>7.5</td>
<td>32768</td>
</tr>
<tr>
<td>18</td>
<td>8</td>
<td>65536</td>
</tr>
<tr>
<td>19</td>
<td>8.5</td>
<td>131072</td>
</tr>
<tr>
<td>20</td>
<td>9</td>
<td>262144</td>
</tr>
<tr>
<td>21</td>
<td>9.5</td>
<td>524288</td>
</tr>
<tr>
<td>22</td>
<td>10</td>
<td>1048576</td>
</tr>
<tr>
<td>23</td>
<td>10.5</td>
<td>2097152</td>
</tr>
<tr>
<td>24</td>
<td>11</td>
<td>4194304</td>
</tr>
<tr>
<td>25</td>
<td>11.5</td>
<td>8388608</td>
</tr>
<tr>
<td>26</td>
<td>12</td>
<td>16777216</td>
</tr>
<tr>
<td>27</td>
<td>12.5</td>
<td>33554432</td>
</tr>
<tr>
<td>28</td>
<td>13</td>
<td>67108864</td>
</tr>
<tr>
<td>29</td>
<td>13.5</td>
<td>134217728</td>
</tr>
<tr>
<td>30</td>
<td>14</td>
<td>268435456</td>
</tr>
<tr>
<td>31</td>
<td>14.5</td>
<td>536870912</td>
</tr>
<tr>
<td>32</td>
<td>15</td>
<td>1073741824</td>
</tr>
</tbody>
</table>

Parameter: No. of bacteria at t=0:
Generation time [hours]:
Order of growth:

![Graph of bacterial growth over time]
Design models with differential equations

Example bacterial growth: bacteria divide 2 times per hour.

→ **Duration** between divisions $D = 0.5$ hours.

→ **Rate** of division $\lambda = 2$ per hour \[ \lambda = \frac{1}{D} \]

"The speed by which the total number of bacteria $B$ changes over time $t$…"

"…is proportional to the individual rate of division $\lambda$ …"

"…and proportional to the number of bacteria reproducing at time $t$"

\[
\frac{dB(t)}{dt} = \lambda B(t)
\]

Integration

\[
B(t) = \text{const} \cdot e^{\lambda t}
\]

Derivative

Total number of bacteria at time $t$
Differential equations offer more…

Previously: the bacterial culture grows indefinitely (unrealistic in a finite world)
Now: the culture cannot exceed a certain capacity $K$ (realistic: test tube)

"The speed by which the total number of bacteria $B$ changes over time $t$ is proportional to the individual rate of division $\lambda$ at time $t$..."

\[
\frac{dB(t)}{dt} = \tilde{\lambda} B(t) \left(1 - \frac{B(t)}{K}\right)
\]

"The growth rate approaches zero when the bacterial culture approaches the value of the capacity ($B(t)=K$)."

\[
B(t) = \frac{B_0 K}{B_0 + (K - B_0)e^{-\tilde{\lambda}t}}
\]
A mathematical Model is just a mathematical way to describe a process.

Simple processes may be intuitively described "by hand"

Differential equations are a useful tool to describe complex processes.

Differential equations allow for describing dynamic processes by means of interpretable parameters.
Exercise 2: preliminary considerations

Assume A) a bacterium which, under optimal conditions, reproduces 2 times per hour (per capita-reproduction rate=2/h) and B) a volume which can harbour at maximum 1,000,000 bacteria.

- Fill in the numbers for the upper and lower bounds of each axis into the white boxes
- Draw a qualitative curve for the per capita-reproduction rate \( \lambda \) and the number of bacteria over time, \( B(t) \). Where is the inflection point of \( B(t) \)?
Exercise 2: First steps

- Aim: first steps with modeling software
- Complete file "00_bactGrowth.txt" with the equations of the bacterial growth curve (save your work), and specify the initial value B(0).
- Copy the text into the program editor of Berkeley-Madonna
- Click "Run"
- Make your sliders in Menu Parameters|Define Sliders...
- Verify the preliminary considerations of the previous slide
Program

Lesson 2

Deterministic models: SIR-model, theory, basic reproduction number $R_0$, epidemic vs. endemic case
SIR-Model

Extensions of the SIR-model:
- SIRS
- SEIR
- SEIRS

Polio virus type 1

Common way of representing a model: Compartments & Transitions

Susceptible \( S \) \rightarrow Infectious \( I \) \rightarrow immune \( R \)
Information needed

• Durations: latent and infectious period
• Rates: contact rate(s)
• Probabilities: \( P(\text{infection} \mid \text{transmission}) \)
• Demography: birth and death rate, age structure of the population
• Disease: Proportion of inapparent infections
• ....
Birth of (susceptible) individuals

\[
dS(t) / dt = \mu [S(t) + I(t) + R(t)] = 1
\]

- **S**: Proportion susceptibles
- **\(\mu\)**: Per capita birth rate
Dynamic description: Infection

\[ \frac{dS(t)}{dt} = \mu - \beta c I(t) S(t) \]

\[ \frac{dI(t)}{dt} = \beta c I(t) S(t) \]

- S: Proportion susceptible
- I: Proportion infectious
- R: Proportion immune

\( \mu \): Per capita birth rate
\( \beta \): Contact rate
\( c \): P (infection | contact)
Mass action law

The probability of encounterings between susceptible and infectious individuals depends on:
- the contact rate $\beta$ ("Temperature")
- the ratio Susceptible : Infectious

\[
\begin{align*}
S^2 &\quad 2(S\cdot I) \\
I^2 &\quad \text{Sum}
\end{align*}
\]
Dynamic description: Infection

\[
\begin{align*}
\text{new infections} \\
\frac{dS(t)}{dt} &= \mu - \beta c I(t) S(t) \\
\frac{dI(t)}{dt} &= \beta c I(t) S(t)
\end{align*}
\]

- **S** Proportion susceptible
- **I** Proportion infectious
- **R** Proportion immune

- \(\mu\) Per capita birth rate
- \(\beta\) Contact rate
- \(c\) P (infection | contact)
Dynamic description: Loss of infection

\[
\begin{align*}
\frac{dS(t)}{dt} &= \mu - \beta c \ I(t) \ S(t) \\
\frac{dI(t)}{dt} &= \beta c \ I(t) \ S(t) - \gamma I(t) \\
\frac{dR(t)}{dt} &= \gamma I(t)
\end{align*}
\]

- \( S \) Proportion susceptible
- \( I \) Proportion infectious
- \( R \) Proportion immune
- \( \mu \) Per capita birth rate
- \( \beta \) Contact rate
- \( \gamma \) Rate of loss of infectiousness
- \( c \) Probability of infection given a contact
Dynamic description: Mortality

\[
\begin{align*}
\frac{dS(t)}{dt} &= \mu - \beta c I(t) S(t) - \mu S(t) \\
\frac{dI(t)}{dt} &= \beta c I(t) S(t) - \gamma I(t) - \mu I(t) \\
\frac{dR(t)}{dt} &= \gamma I(t) - \mu R(t)
\end{align*}
\]

- **S** Proportion susceptible
- **I** Proportion infectious
- **R** Proportion immune
- \(\mu\) Per capita birth rate
- \(\beta\) Contact rate
- \(c\) \(P\) (infection | contact)
- \(\gamma\) Rate of loss of infectiousness
Numeric solution of the model

• **Initialisation**
  - choose parameter values for $\beta$, $c$, $\gamma$ and $\mu$
  - choose initial values for $S(0)$, $I(0)$, and $R(0)$

• **First iteration (time = 0)**
  - compute for a short time step $\Delta$ the changes $dS(0)/dt$, $dI(0)/dt$ and $dR(0)/dt$
  - extrapolate changes to $S(0+\Delta)$, $I(0+\Delta)$ and $R(0+\Delta)$

• **Following iterations (time = t)**
  1. compute for a short time step $\Delta$ the changes $dS(t)/dt$, $dI(t)/dt$ and $dR(t)/dt$
  2. extrapolate changes to $S(t+\Delta)$, $I(t+\Delta)$ and $R(t+\Delta)$

$t=t+\Delta$, goto 1

A ready-to-use software of the SIR model is available from www.uni-tuebingen.de/modeling/Mod_Pub_Software_SIR_en.html
Exercise 3: preliminary considerations

The SIR model, defined as,

\[
\begin{align*}
    \frac{dS(t)}{dt} &= \mu - \beta c I(t) S(t) - \mu S(t) \\
    \frac{dI(t)}{dt} &= \beta c I(t) S(t) - \gamma I(t) - \mu I(t) \\
    \frac{dR(t)}{dt} &= \gamma I(t) - \mu R(t)
\end{align*}
\]

produces qualitatively a graph like

Draw your qualitative prediction into the graph on how the course of the epidemic would change (higher, faster, slower, etc) if

- the contact rate between people increases? \((\beta \uparrow)\)
- patients recover more rapidly? \((\gamma \uparrow)\)
- \(\beta\) and \(\gamma\) increase at the same time

Aim: understanding the role of the parameters in the SIR
Exercise 3: solving differential equations numerically

• Aim: quantitative epidemiology of infectious diseases – learning by doing

• Complete file "10_SIR.txt" with the equations of the SIR-model (save your work), and specify the initial values (INIT S, I, R).

• Copy the text into the program editor of Berkeley-Madonna

• Click "Run"
Exercise 3:

Make your sliders in Menu Parameters|Define Sliders...

... and verify your preliminary considerations of the previous slide
$R_0$: Basic reproduction number

- Average number of secondary infections which one infectious individual would cause in a fully susceptible population

**Definition:** $R_0 = \beta c D$

- $R_0 > 1$: Infection can persist; an endemic state is possible
- $R_0 < 1$: Infection cannot persist; goes extinct

$D = 1 / (\gamma + \mu)$ average duration of the infectious period

$\beta c$ Number of (sufficiently close) contacts per unit of time
$R_0$ for some infectious diseases

<table>
<thead>
<tr>
<th>Disease</th>
<th>Average age at infection [years]</th>
<th>$R_0$</th>
<th>Critical vaccination coverage $p_{\text{crit}}$ [%]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Measles</td>
<td>5.0</td>
<td>15.6</td>
<td>94</td>
</tr>
<tr>
<td>Pertussis</td>
<td>4.5</td>
<td>17.5</td>
<td>94</td>
</tr>
<tr>
<td>Mumps</td>
<td>7.0</td>
<td>11.5</td>
<td>91</td>
</tr>
<tr>
<td>Rubella</td>
<td>10.2</td>
<td>7.2</td>
<td>86</td>
</tr>
<tr>
<td>Polio</td>
<td>10.4</td>
<td>6.1</td>
<td>84</td>
</tr>
<tr>
<td>Diphtheria</td>
<td>10.4</td>
<td>6.1</td>
<td>84</td>
</tr>
</tbody>
</table>
**Epidemic**

*SIR Model; without births and deaths*

\[ \beta c = 0.5/\text{day}, \quad \gamma = 0.1/\text{day}, \quad \mu = 0/\text{day} \quad \Rightarrow \quad R_0 = 5 \]
SIR Model; without births and deaths

\[ \beta_c = 0.2 / \text{Tag}, \quad \gamma = 0.1 / \text{Tag}, \quad \mu = 0 / \text{Tag} \Rightarrow R_0 = 2 \]
At the end of an Epidemic...

... susceptible individuals may remain
Proportion $S_\infty$ susceptible at the end of the epidemic

\[- \log (S_\infty) = R_0 \ (1 - S_\infty)\]
Exercise 4: endemic infection

- Make sure that slider settings in file "11_SIRreparameterized.mmd" are as follows

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Minimum</th>
<th>Use</th>
<th>Maximum</th>
</tr>
</thead>
<tbody>
<tr>
<td>STOPTIME</td>
<td>0</td>
<td>100</td>
<td>5000</td>
</tr>
<tr>
<td>DT</td>
<td>0</td>
<td>0.1</td>
<td>1</td>
</tr>
<tr>
<td>DTOUT</td>
<td>0</td>
<td>1</td>
<td>10</td>
</tr>
<tr>
<td>inInfected</td>
<td>0</td>
<td>0.0001</td>
<td>1</td>
</tr>
<tr>
<td>lifeExpectYears</td>
<td>0</td>
<td>50</td>
<td>100</td>
</tr>
<tr>
<td>durationInfected</td>
<td>0</td>
<td>10</td>
<td>20</td>
</tr>
<tr>
<td>R0</td>
<td>0</td>
<td>15</td>
<td>20</td>
</tr>
</tbody>
</table>

- For $R_0=15$ (Measles-like) simulate an extended period of time by increasing STOPTIME from 100 to 5000 days (=13.7 years)
- Simulate a population with a lower life expectancy (developing countries) by decreasing lifeExpectYears from 50 to 30 years.

- What is the reason for recurrent epidemics?
- Why is the time between epidemics reduced?
Endemic case

*SIR Modell with demography*

\[ \beta c = 0.5/\text{day}, \quad \gamma = 0.1/\text{day}, \quad \mu = 0.0005/\text{day} \Rightarrow R_0 = 5 \]
Summary

- **Neglecting births and deaths,**
  - we model an *epidemic* scenario;
  - after the epidemic, a proportion of susceptibles, which depends on $R_0$, remains

- **Considering births and deaths,**
  - we model an *endemic* scenario
  - the model variables ($S,I,R,...$) approach the endemic state (if $R_0 > 1$);
  - the equilibrium prevalence depends on $R_0$. 
Vaccination:
final size of an epidemic,
critical vaccination coverage
Dynamic description: SIR without vaccination

Model without vaccination

\[
\begin{align*}
\frac{dS(t)}{dt} &= \mu - \beta c I(t) S(t) - \mu S(t) \\
\frac{dI(t)}{dt} &= \beta c I(t) S(t) - \gamma I(t) - \mu I(t) \\
\frac{dR(t)}{dt} &= \gamma I(t) - \mu R(t)
\end{align*}
\]

- S: Proportion susceptible
- I: Proportion infectious
- R: Proportion immune

- \mu: Per capita birth rate
- \beta: Contact rate
- c: P (infection | contact)
- \gamma: Rate of loss of infectiousness
Dynamic description: SIR with vaccination

A proportion of newborns will be vaccinated

\[
dS(t) / dt = \mu (1-p) - \beta c I(t) S(t) - \mu S(t)
\]
\[
dI(t) / dt = \beta c I(t) S(t) - \gamma I(t) - \mu I(t)
\]
\[
dR(t) / dt = \mu p + \gamma I(t) - \mu R(t)
\]

S  Proportion susceptible  \( \mu \)  Per capita birth rate  c  P (infection | contact)
I  Proportion infectious  \( \beta \)  Contact rate  p  Proportion vaccinated
R  Proportion immune  \( \gamma \)  rate of loss of infectiousity
Exercise 5: Vaccination

Aim: Understanding the concept of thresholds

- Implement parameter \( p \) for the proportion of vaccinated newborns (see previous slide) in the equations of file "11_SIRreparameterized.txt" file and save it as "12_SIRvaccination.txt"

- Define slider for \( p \) in Menu
  Parameters|Define Sliders... and choose slider settings as shown in the screenshot on the right
Exercise 5: Vaccination

Aim: Understanding the concept of thresholds

- Technical remark: For purposes of better inspection, we change in the output window axis settings for compartment $I$ to "Auto" – see below and ask the lecturer.

1. [Diagram of Choose Variables window showing selection of variables]

2. [Diagram of Axis Settings window showing settings for X and Y axes]
Exercise 5: Vaccination

Aim: Understanding the concept of thresholds

- For $R_0 = 15$, increase $p$ up to a value when there is no epidemic anymore. This is the critical vaccination coverage $p^*$. Repeat the procedure for $R_0 = 10, 5, \text{ and } 2$, and plot your results in the graph to the right.

What is the critical vaccination coverage when the basic reproduction number tends to values of $R_0 \to 1$?
Endemic equilibrium

no change of model variables in the endemic equilibrium

\[
\begin{align*}
0 &= \mu (1-p) - \beta c I(t) S(t) - \mu S(t) \\
0 &= \beta c I(t) S(t) - \gamma I(t) - \mu I(t) \\
0 &= \mu p + \gamma I(t) - \mu R(t)
\end{align*}
\]

S  Proportion susceptible  \( \mu \)  Per capita birth rate  c  P (infection | contact)
I  Proportion infectious  \( \beta \)  Contact rate  p  Proportion vaccinated
R  Proportion immune  \( \gamma \)  rate of loss of infectiousity
Endemic equilibrium

no change of model variables in the endemic equilibrium

\[
0 = \mu (1-p) - \beta c I S - \mu S
\]

\[
0 = \beta c S - \gamma - \mu
\]

\[
0 = \mu p + \gamma I - \mu R
\]

S  Proportion susceptible  \mu  Per capita birth rate  c  P (infection | contact)
I  Proportion infectious  \beta  Contact rate  p  Proportion vaccinated
R  Proportion immune  \gamma  rate of loss of infectiosity
Endemic equilibrium

Estimate $R_0$ from the proportion of susceptibles in the endemic equilibrium

\[ S = \frac{(\gamma + \mu)}{(\beta c)} = \frac{1}{R_0} \]
\[ I = (1 - \frac{1}{R_0} - p) \frac{\mu}{(\gamma + \mu)} \]
\[ R = 1 - S - I \]

- $S$: Proportion susceptible
- $\mu$: Per capita birth rate
- $c$: $P$ (infection | contact)
- $\beta$: Contact rate
- $p$: Proportion vaccinated
- $\gamma$: Rate of loss of infectiousness
Critical vaccination coverage

Parameters of the right hand side are known, except $p$

$I = (1 - 1/R_0 - p) \mu / (\gamma + \mu)$

- $I$ Proportion infectious
- $\mu$ Per capita birth rate = death rate
- $p$ Proportion vaccinated
- Basic reproduction number: $R_0 = \beta c / (\gamma + \mu)$
- $\gamma$ rate of loss of infectiousity
Critical vaccination coverage

Parameters of the right hand side are known, except $p$

$$0 = \left(1 - \frac{1}{R_0} - p_{\text{crit}}\right) \frac{\mu}{(\gamma + \mu)}$$

$\iff$ $p_{\text{crit}} = 1 - \frac{1}{R_0} = 1 - S$

To eliminate a disease, it is not necessary to vaccinate the whole population.
Critical vaccination coverage

![Graph showing the relationship between basic reproduction number (R0) and proportion vaccinated, with shaded regions indicating elimination and persistence.](image-url)
Summary

- The proportion of susceptibles in the endemic equilibrium does not depend on the proportion $p$ of vaccinated children.
- Transmission stops if $p \geq p_{\text{crit}}$.
- The critical vaccination coverage is $p_{\text{crit}} = 1 - 1/R_0$.

- The model can be used for sensitivity analyses into the effects of different vaccination strategies:
  - What is the critical vaccination coverage?
  - How does vaccination impact on the prevalence and incidence of the infection?
  - What is the best vaccination strategy (e.g., ring vaccination vs. mass vaccination)?
Estimation of model parameters

\[ \mu \] Per capita birth rate = death rate
\[ 1 / \mu \] is the life expectancy

\[ \gamma \] Loss-of-infection rate
\[ 1 / (\gamma + \mu) \] is the average duration of the infectious period

\[ R_0 \] Basic reproduction number
\[ 1 / R_0 \] is the endemic prevalence of susceptibles

\[ p_{\text{crit}} \] Critical vaccination coverage
\[ p_{\text{crit}} = 1 - 1 / R_0 \]

\[ \beta_c \] Effective contact rate
\[ \beta_c = R_0 (\gamma + \mu) \]
### Vergleich: deterministische vs. stochastische Modelle

<table>
<thead>
<tr>
<th>Deterministische Modelle</th>
<th>stochastische Modelle</th>
</tr>
</thead>
<tbody>
<tr>
<td>• werden i.d.R. durch explizite Formeln (Differenzialgleichungen) erstellt</td>
<td>• werden i.d.R. durch (individuen-basierte) Simulationsprogramme erstellt</td>
</tr>
<tr>
<td>• liefern bei gleichen Anfangsbedingungen stets identische Ergebnisse</td>
<td>• liefern bei gleichen Anfangsbedingungen zufallsbedingt unterschiedliche Ergebnisse</td>
</tr>
<tr>
<td>• ihre Ergebnisse sind meist besser verallgemeinerbar</td>
<td>• ihre Ergebnisse sind meist realitätsnäher da sie zufällige Effekte wiedergeben können (Stochastizität)</td>
</tr>
<tr>
<td>→ Zur Planung von Interventionsmaßnahmen sind deterministische Modelle oft besser geeignet</td>
<td>• Für die Untersuchung von Effekten in kleinen Populationen besser</td>
</tr>
</tbody>
</table>
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