Modeling the Spreading of Diseases

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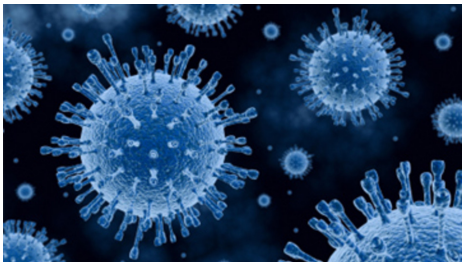


0.1 Plan for week 46-47

Monday 15/11:

- Exercise E.29, E.49
- Modeling infectious diseases
  - The SIR model (repetition from last week)
  - Extensions of the SIR model

Thursday 18/11:

- No lecture (probably)

Week 47:

- Monday: Project lecture/questions
- Thursday: Project help ("orakel").

0.2 We shall model a complex phenomenon by simple math

Plan:

- Use simple intuition to derive a system of *difference equations* to model the spread of diseases
- Program the difference equations in the usual way (i.e. `for`-loops)
- Transform the difference equations to *ordinary differential equations*
- Explore possible model extensions

0.3 Assumptions:

- We consider a perfectly mixed population in a confined area
- No spatial transport, just temporal evolution
- We do not consider individuals, just a grand mix of them

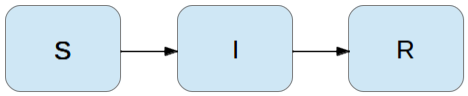
We consider very simple models, but these can be extended to full models that are used world-wide by health authorities. Typical diseases modeled are flu, measles, swine flu, HIV, SARS, ebola, Covid19, ...

0.4 We keep track of 3 categories in the SIR model

- **S**: susceptibles - who can get the disease
- **I**: infected - who have developed the disease and infect susceptibles
- **R**: recovered - who have recovered and become immune

Mathematical quantities: $S(t)$, $I(t)$, $R(t)$: no of people in each category

Goal: Find and solve equations for $S(t)$, $I(t)$, $R(t)$



0.5 The traditional modeling approach is very mathematical - our idea is to model, program and experiment

- Numerous books on mathematical biology treat the SIR model
- Quick modeling step (max 2 pages)
- Nonlinear differential equation model
- Cannot solve the equations, so focus is on discussing stability (eigenvalues), qualitative properties, etc.
- Very few extensions of the model to real-life situations

0.6 Dynamics in a time interval Δt: people move from S to I

S-I interaction:

- In a total population of N people, with S susceptibles and I infected, the chance of a single person in S meeting a person in I is proportional to I/N.
- The total number of such meetings will be proportional to SI/N. A certain fraction of these meetings leads to disease transmission.
- In a (small) time interval Δt, we assume that $\beta \Delta t SI/N$ meetings where the infected "successfully" infects the susceptible
- This gives a loss $\Delta t\, \beta SI/N$ in the S category and a corresponding gain in the I category

Remark. It is reasonable that the fraction depends on Δt (twice as many infected in $2\Delta t$ as in Δt). β is some unknown parameter we must measure, supposed to not depend on Δt, but maybe time t. β lumps *a lot* of biological and sociological effects into one number.

0.7 The equations describing S-I interaction become

Loss in $S(t)$ from time t to $t + \Delta t$:

$$S(t + \Delta t) = S(t) - \Delta t\, \beta \frac{S(t)I(t)}{N}$$

Gain in $I(t)$:

$$I(t + \Delta t) = I(t) + \Delta t\, \beta \frac{S(t)I(t)}{N}$$

0.8 Modeling the transition from I to R

I-R transition:

- After some days, the infected has recovered and moves to the R category
- A simple model: in a small time Δt (say 1 day), a fraction $\Delta t\, \nu$ of the infected are removed (ν must be measured)

We must subtract this fraction in the balance equation for I:

$$I(t + \Delta t) = I(t) + \Delta t\, \beta S(t)I(t) - \Delta t\, \nu I(t)$$

The loss $\Delta t\, \nu I$ is a gain in R:

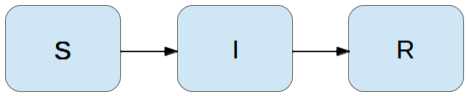
$$R(t + \Delta t) = R(t) + \Delta t\, \nu I(t)$$

0.9 We have three equations for S, I, and R

$$S(t + \Delta t) = S(t) - \Delta t\, \beta \frac{S(t)I(t)}{N} \tag{1}$$

$$I(t + \Delta t) = I(t) + \Delta t\, \beta \frac{S(t)I(t)}{N} - \Delta t \nu I(t) \tag{2}$$

$$R(t + \Delta t) = R(t) + \Delta t\, \nu I(t) \tag{3}$$



Before we can compute with these, we must

- know β and ν
- know $S(0)$ (many), $I(0)$ (few), $R(0)$ (0?)
- choose Δt

0.10 The computation involves just simple arithmetics

- Set $\Delta t = 0.1$ (= 6 minutes)
- Set $\beta = 0.06$, $\nu = 0.008333$
- Set $S(0) = 50$, $I(0) = 1$, $R(0) = 0$

$$
\begin{aligned}
S(\Delta t) &= S(0) - \Delta t\,\beta\frac{S(0)I(0)}{N} \approx 49.99 \\
I(\Delta t) &= I(0) + \Delta t\,\beta\frac{S(0)I(0)}{N} - \Delta t\,\nu I(0) \approx 1.002 \\
R(\Delta t) &= R(0) + \Delta t\,\nu I(0) \approx 0.0008333
\end{aligned}
$$

- We can continue, but quickly gets boring...
- Solve with a for-loop as usual

0.11 We use the standard notation

$$S^n = S(n\Delta t), \quad I^n = I(n\Delta t), \quad R^n = R(n\Delta t)$$

$$S^{n+1} = S((n+1)\Delta t), \quad I^{n+1} = I((n+1)\Delta t), \quad R^{n+1} = R((n+1)\Delta t)$$

The equations can now be written more compactly (and computer friendly):

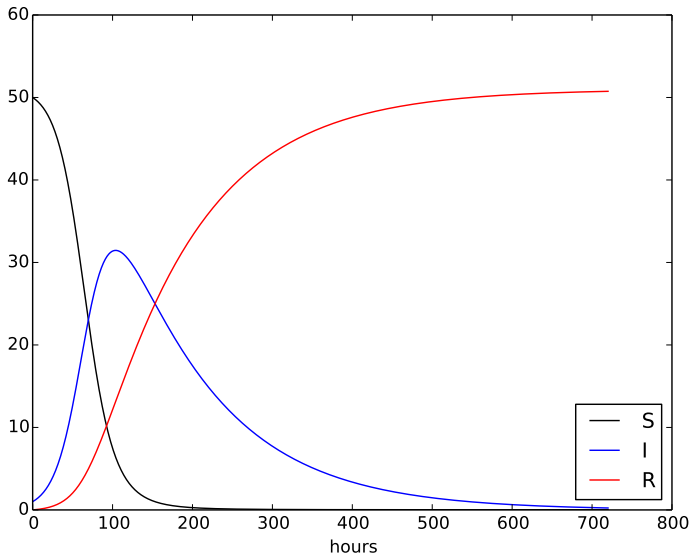
$$
\begin{aligned}
S^{n+1} &= S^n - \Delta t\,\beta S^n I^n/N && (4)\\
I^{n+1} &= I^n + \Delta t\,\beta S^n I^n/N - \Delta t\,\nu I^n && (5)\\
R^{n+1} &= R^n + \Delta t\,\nu I^n && (6)
\end{aligned}
$$

0.12 Store S,I,R in arrays and solve with a loop

```
import numpy as np
import matplotlib.pyplot as plt

beta = 0.06
nu =0.008333
dt = 0.1              # 6 min (time measured in hours)
D = 30                # simulate for D days
Steps = int(D*24/dt)      # corresponding no of hours

t = np.linspace(0, Steps*dt, Steps+1)
S = np.zeros(Steps+1)
I = np.zeros(Steps+1)
R = np.zeros(Steps+1)

S[0] = 50
I[0] = 1
```

```
N = S[0]+I[0]  #total population

for n in range(Steps):
    S[n+1] = S[n] - dt*beta*S[n]*I[n]/N
    I[n+1] = I[n] + dt*beta*S[n]*I[n]/N - dt*nu*I[n]
    R[n+1] = R[n] + dt*nu*I[n]

# Plot the graphs
plt.plot(t, S, 'k-', t, I, 'b-', t, R, 'r-')
plt.legend(['S', 'I', 'R'], loc='lower right')
plt.xlabel('hours')
plt.show()
```

0.13 We have predicted a disease!



0.14 The standard mathematical approach: ODEs

We had from intuition established

$$
\begin{aligned}
S(t+\Delta t) &= S(t) - \Delta t\,\beta\frac{S(t)I(t)}{N} \\
I(t+\Delta t) &= I(t) + \Delta t\,\beta\frac{S(t)I(t)}{N} - \Delta t\,\nu I(t) \\
R(t+\Delta t) &= R(t) + \Delta t\,\nu R(t)
\end{aligned}
$$

The mathematician will now make *differential equations*. Divide by Δt and rearrange:

$$\frac{S(t+\Delta t)-S(t)}{\Delta t} = -\beta\frac{S(t)I(t)}{N}$$
$$\frac{I(t+\Delta t)-I(t)}{\Delta t} = \beta t\frac{S(t)I(t)}{N} - \nu I(t)$$
$$\frac{R(t+\Delta t)-R(t)}{\Delta t} = \nu R(t)$$

0.15 A derivative arises as $\Delta t \to 0$

If we let $\Delta t \to 0$, we get derivatives on the left-hand side:

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

This is a system of differential equations for the functions $S(t)$, $I(t)$, $R(t)$. For a unique solution, we need $S(0)$, $I(0)$, $R(0)$.

0.16 The ODE system cannot be solved analytically

Recall the Forward Euler method: Approximate the derivative with a *finite difference*, e.g.,

$$S'(t) \approx \frac{S(t+\Delta t)-S(t)}{\Delta t}$$

and rearrange to get formulas like

$$S(t+\Delta t) = S(t) - \Delta t\,\beta S(t)I(t).$$

This brings us back to the first model, which we solved using a `for`-loop.

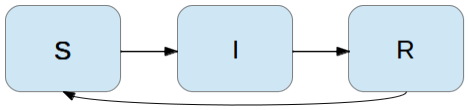
0.17 Or use a prebuilt solver like `ODESolver`

Implement the right hand side of the ODE system as a Python function:

```
def SIR_model(u,t):
    beta = 0.06
    nu = 0.008333
    S, I, R = u[0], u[1], u[2]
    N = S+I+R
    dS = -beta*S*I/N
    dI = beta*S*I/N - nu*I
    dR = nu*I
    return [dS,dI,dR]
```

0.18 Let us extend the model: no life-long immunity

Assumption. After some time, people in the R category lose the immunity. In a small time Δt this gives a leakage $\Delta t\,\gamma R$ to the S category. ($1/\gamma$ is the mean time for immunity.)

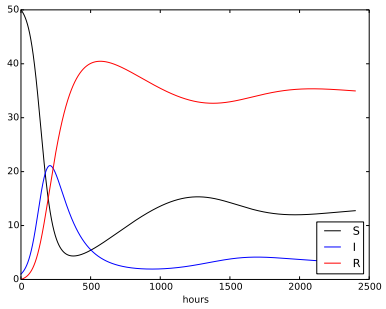


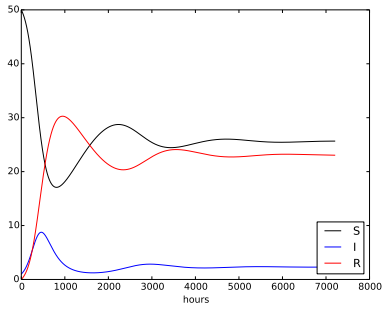
$$S'(t) = -\beta \frac{S(t)I(t)}{N} + \gamma R$$
$$I'(t) = \beta t \frac{S(t)I(t)}{N} - \nu I(t)$$
$$R'(t) = \nu R(t) - \gamma R$$

No complications in the computational model!

0.19 The effect of loss of immunity

$1/\gamma = 50$ days. β reduced by 2 and 4 (left and right, resp.):

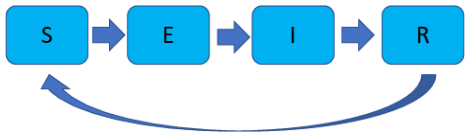




0.20 Adding more categories: the SEIR model

- Diseases have an *incubation period*, a delay from when a person gets infected until he/she has symptoms and can infect others
- For some applications, it is important to include the incubation period in the models

- Add a new category E (for exposed).
- People move from S to E as they are infected, then from E to I



0.21 Equations of the SEIR model

$$
\begin{aligned}
S'(t) &= -\beta SI/N + \gamma R, \\
E'(t) &= \beta SI/N - \mu E, \\
I'(t) &= \mu E - \nu I, \\
R'(t) &= \nu I - \gamma R.
\end{aligned}
$$

0.22 The SEIR model implemented as a function

```
def SEIR(u,t):
    S, E, I, R = u
    N = S+I+R+E
    beta=1.0; mu=1.0/5
    nu=1.0/7; gamma=1.0/50
    dS = -beta*S*I/N + gamma*R
    dE  = beta*S*I/N - mu*E
    dI =  mu*E - nu*I
    dR = nu*I - gamma*R
    return [dS,dE,dI,dR]
```

0.23 Parameter estimation is needed for predictive modeling

- Any small Δt will do
- One can reason about μ, ν, γ:
  - $1/\mu$ is the mean incubation time
  - $1/\nu$ is the mean recovery
  - $1/\gamma$ is mean duration of immunity
- β is more complex, since it depends both on the disease and how people behave

So, what if we don't know β?

- Can still learn about the *dynamics* of diseases
- Can find the sensitivity to and influence of β
- Can apply *parameter estimation* procedures to fit β to data

0.24 A class is convenient for models with parameters

- The `SEIR`-function has all parameters explicitly defined in the code
- If we want to solve the model for multiple parameters, it is more convenient to implement it as a class
- A constructor (`__init__`) to set all the parameters, a `__call__` method to implement the ODE system

0.25 Class implementation of the SEIR model

```
class SEIR:
    def __init__(self, beta, mu, nu, gamma):
        self.beta = beta
        self.mu = mu
        self.nu = nu
        self.gamma = gamma


    def __call__(self,u,t):
        S, E, I, R = u
        N = S+I+R+E
        dS = -self.beta*S*I/N + self.gamma*R
        dE  = self.beta*S*I/N - self.mu*E
        dI =  self.mu*E - self.nu*I
        dR = self.nu*I - self.gamma*R
        return [dS,dE,dI,dR]
```

0.26 Summary

- The SIR model is a classic framework for modeling spread of diseases
- Easy to extend with more features, more dynamics and compartments
- Different versions; difference equations, ODEs, stochastic models all based on the same fundamental ideas
- Parameters are directly linked to disease characteristics such as recovery time and reproduction numbers
- Not all parameters are easy to estimate, makes model-based prediction challenging in practice