Modeling the Spreading of Diseases

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We shall model a very complex phenomenon by simple math....

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 (cf. statistical mechanics vs thermodynamics)

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, ...

All these slides and associated programs are available from https://github.com/hplgit/disease-modeling.

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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)

$$S \longrightarrow R$$

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

Dynamics in a time interval Δt : $\Delta t \beta SI$ people move from S to I

S-I interaction:

- In a mix of S and I people, there are SI possible pairs
- A certain fraction $\Delta t \beta$ of SI meet in a (small) time interval Δt , with the result that the infected "successfully" infects the susceptible
- The loss $\Delta t \, \beta SI$ in the S catogory is 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.

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For practical calculations, we must express the S-I interaction with symbols

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

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

Gain in I(t):

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

Modeling the interaction between R and I

R-I interaction:

- 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:

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

We have three equations for S, I, and R

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

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

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



Before we can compute with these, we must

- ullet know eta and u
- know S(0) (many), I(0) (few), R(0) (0?)
- choose Δt

- Set $\Delta t = 6$ minutes
- Set $\beta = 0.0013$, $\nu = 0.8333$
- Set S(0) = 50, I(0) = 1, R(0) = 0

$$S(\Delta t) = S(0) - \Delta t \,\beta S(0)I(0) \approx 49.99$$

$$I(\Delta t) = I(0) + \Delta t \,\beta S(0)I(0) - \Delta t \,\nu I(0) \approx 1.002$$

$$R(\Delta t) = R(0) + \Delta t \,\nu I(0) \approx 0.0008333$$

- In reality, S, I, R are integers and events are discrete (meet, get sick)
- In the model, we work with real numbers and continuous events
- Reasonable approximation in a not too small population

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- Reasonable approximation in a not too small population

And we can continue...

$$S(2\Delta t) = S(\Delta t) - \Delta t \,\beta S(\Delta t) I(\Delta t) \approx 49.87$$

$$I(2\Delta t) = I(\Delta t) + \Delta t \,\beta S(\Delta t) I(\Delta t) - \Delta t \,\nu I(\Delta t) \approx 1.011$$

$$R(2\Delta t) = R(\Delta t) + \Delta t \,\nu I(\Delta t) \approx 0.00167$$

Repeat...

$$S(3\Delta t) = S(2\Delta t) - \Delta t \,\beta S(2\Delta t)I(2\Delta t) \approx 49.98$$

$$I(3\Delta t) = I(2\Delta t) + \Delta t \,\beta S(2\Delta t)I(2\Delta t) - \Delta t \,\nu I(2\Delta t) \approx 1.017$$

$$R(3\Delta t) = R(2\Delta t) + \Delta t \,\nu I(2\Delta t) \approx 0.0025$$

But this is getting boring! Let's ask a computer to do the work!

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But this is getting boring! Let's ask a computer to do the work!

First, some handy 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):

$$S^{n+1} = S^n - \Delta t \,\beta S^n I^n \tag{4}$$

$$I^{n+1} = I^n + \Delta t \, \beta S^n I^n - \Delta t \, \nu I^n \tag{5}$$

$$R^{n+1} = R^n + \Delta t \, \nu I^n \tag{6}$$

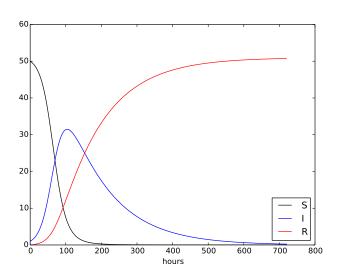
With variables, arrays, and a loop we can program

```
Suppose we want to compute until t = N\Delta t, i.e., for
n = 0, 1, \dots, N - 1. We can store S^0, S^1, S^2, \dots, S^N in an array
(or list).
Python (Matlab):
 t = linspace(0, N*dt, N+1) # all time points
 S = zeros(N+1)
 I = zeros(N+1)
 R = zeros(N+1)
 for n in range(N):
     S[n+1] = S[n] - dt*beta*S[n]*I[n]
     I[n+1] = I[n] + dt*beta*S[n]*I[n] - dt*nu*I[n]
     R[n+1] = R[n] + dt*nu*I[n]
```

Here is the complete program

```
beta = 0.0013
n_{11} = 0.8333
dt = 0.1
                   # 6 min (time measured in hours)
D = 30
                    # simulate for D days
N = int(D*24/dt) # corresponding no of hours
from numpy import zeros, linspace
t = linspace(0, N*dt, N+1)
S = zeros(N+1)
I = zeros(N+1)
R = zeros(N+1)
for n in range(N):
    S[n+1] = S[n] - dt*beta*S[n]*I[n]
    I[n+1] = I[n] + dt*beta*S[n]*I[n] - dt*nu*I[n]
    R[n+1] = R[n] + dt*nu*I[n]
# Plot the graphs
from matplotlib.pyplot import *
plot(t, S, 'k-', t, I, 'b-', t, R, 'r-')
legend(['S', 'I', 'R'], loc='lower right')
xlabel('hours')
show()
```

We have predicted a disease!



How much math and programming did we use?

Math:

- Plain arithmetics
- The concept of a graph (i.e., discrete function in time)
- Units
- Greek letters

Programming:

- Variable
- Array
- Loop
- Plotting

Detour: The standard mathematical approach

We had from intuition established

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

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

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

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

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

A derivative arises as $\Delta t \rightarrow 0$

In any calculus book, the derivative of S at t is defined as

$$S'(t) = \lim_{t \to 0} \frac{S(t + \Delta t) - S(t)}{\Delta t}$$

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

$$S'(t) = -\beta S(t)I(t)$$

$$I'(t) = \beta tS(t)I(t) - \nu I(t)$$

$$R'(t) = \nu R(t)$$

This is a 3x3 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).

Bad news: we cannot solve these equations!

Time to ask a numerical methods expert:

Replace the derivative with a finite difference, e.g.,

$$S'(t)pprox rac{S(t+\Delta t)-S(t)}{\Delta t}$$

which is accurate for small Δt .

This brings us back to the first model, which we can solve on a computer!

Parameter estimation is needed for predictive modeling

- Any small Δt will do
- One can reason about ν and say that $1/\nu$ is the mean recovery time for the disease (e.g., 1 week for a flu)
- $oldsymbol{\circ}$ eta must in some way be measured, but we don't know what it means...

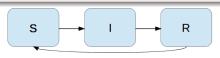
So, what if we don't know β ?

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

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/ γ is the mean time for immunity.)



$$S^{n+1} = S^n - \Delta t \, \beta S^n I^n + \Delta t \, \gamma R^n \tag{7}$$

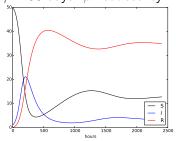
$$I^{n+1} = I^n + \Delta t \,\beta S^n I^n - \Delta t \,\nu I^n \tag{8}$$

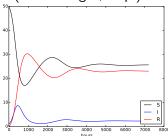
$$R^{n+1} = R^n + \Delta t \, \nu R^n - \Delta t \, \gamma R^n \tag{9}$$

No complications in the computational model!

The effect of loss of immunity

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

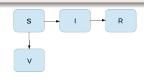




What is the effect of vaccination?

Assumptions

A fraction p of the S category, per time unit, is vaccinated with success. Then in time Δt , $p\Delta tS$ will move to a vaccinated category, V. This does not affect the I and R categories.



$$S^{n+1} = S^n - \Delta t \,\beta S^n I^n + \Delta t \,\gamma R^n - p \Delta t S^n \tag{10}$$

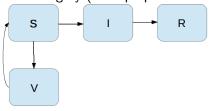
$$V^{n+1} = V^n + p\Delta t S^n \tag{11}$$

$$I^{n+1} = I^n + \Delta t \,\beta S^n I^n - \Delta t \,\nu I^n \tag{12}$$

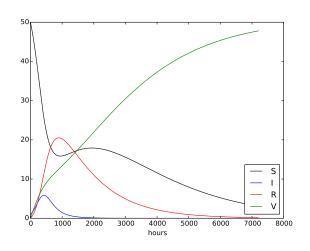
$$R^{n+1} = R^n + \Delta t \, \nu R^n - \Delta t \, \gamma R^n \tag{13}$$

Many possibilities for adjusting the model...

The effect of vaccination decreases over time, so we may move people back to the S category (term proportional to ΔtV).



Effect of adding vaccination



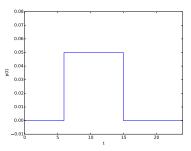
$$(p = 0.0005)$$

What is the effect of an intensive vaccination campaign?

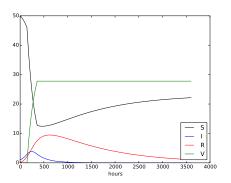
10 times more intense vaccination for 10 days, 6 days after outbreak:

$$p(t) = \left\{ egin{array}{ll} 0.005, & 6 \leq t \leq 15, \\ 0, & ext{otherwise} \end{array}
ight.$$

Implementation: Let p^n be an array as V^n . Set $p^n = 0.05$ for $n = 6 \cdot 24/0.1, \ldots, 15 \cdot 24/0.1$ (days $\cdot 24/\Delta t$, 24 is hours per day).



Effect of vaccination campaign



Note:

- Mathematicians would be scared by the cusps on the curves...
- Could now let the computer run a lot of cases and find the optimal vaccination period

We can experiment with other campaigns



Wearing masks lowers β :

$$\beta(t) = \begin{cases} \beta_1, & 0 \le t < 5, \\ \beta_2 < \beta_1, & t \ge 5 \end{cases}$$

Very easy to implement. (Used to be complicated in differential equation models...)

And now for something similar: zombification!



Zombification: The disease that turns you into a zombie.

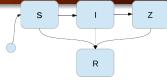
Zombie modeling is almost the same as SIR modeling

Categories

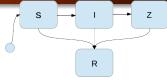
- S: susceptible humans who can become zombies
- 2 I: infected humans, being bitten by zombies
- 3 Z: zombies
- R: removed individuals, either conquered zombies or dead humans

Mathematical quantities: S(t), I(t), Z(t), R(t)

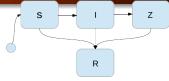
Zombie movie: *The Night of the Living Dead*, Geoerge A. Romero, 1968



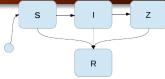
- ① Susceptibles are infected by zombies: $-\Delta t \beta SZ$ in time Δt (cf. the $\Delta t \beta SI$ term in the SIR model).
- ② Susceptibles die naturally or get killed and then enter the removed category. The no of deaths in time Δt is $\Delta t \delta_S S$.
- We also allow new humans to enter the area with zombies (necessary in a war on zombies): $\Delta t \Sigma$ during a time Δt .
- Some infected turn into zombies (Z): Δtρl, while others die (R): δ_IΔtl.
- Nobody from R can turn into Z (important otherwise zombies win).
- **1** Willed zombies go to R: $\Delta t \alpha SZ$.



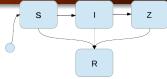
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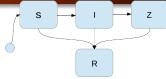
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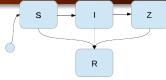
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- **10** We also allow new humans to enter the area with zombies (necessary in a war on zombies): $\Delta t \Sigma$ during a time Δt .
- **②** Some infected turn into zombies (Z): $\Delta t \rho I$, while others die (R): $\delta_I \Delta t I$.
- Nobody from R can turn into Z (important otherwise zombies win).
- **1** Willed zombies go to R: $\Delta t \alpha SZ$.

The four equations in the SIZR model for zombification

$$S^{n+1} = S^{n} + \Delta t \Sigma - \Delta t \beta S^{n} Z - \Delta t \delta_{S} S^{n}$$

$$I^{n+1} = I^{n} + \Delta t \beta S^{n} Z^{n} - \Delta t \rho I^{n} - \Delta t \delta_{I} I^{n}$$

$$Z^{n+1} = Z^{n} + \Delta t \rho I^{n} - \Delta t \alpha S^{n} Z^{n}$$

$$R^{n+1} = R^{n} + \Delta t \delta_{S} S^{n} + \Delta t \delta_{I} I^{n} + \Delta t \alpha S^{n} Z^{n}$$

Interpretation of parameters:

- \bullet Σ : no of new humans brought into the zombified area per unit time.
- β: the probability that a theoretically possible human-zombie pair actually meets physically, during a unit time interval, with the result that the human is infected.
- δ_S: the probability that a susceptible human is killed or dies, in a unit time interval.
- δ_I : the probability that an infected human is killed or dies, in a unit time interval.
- ρ: the probability that an infected human is turned into a zombie, during a unit time interval.
- \bullet α : the probability that, during a unit time interval, a theoretically

Simulate a zombie movie!

Three fundamental phases

- The initial phase (4 h)
- 2 The hysteric phase (24 h)
- The counter attack phase (5 h)



How do we do this? As *p* in the vaccination campaign - the parameters take on different constant values in different time intervals.

H. P. Langtangen, K.-A. Mardal and P. Røtnes: Escaping the Zombie Threat by Mathematics, in A. Whelan et al.: *Zombies in the Academy - Living Death in Higher Education*, University of Chicago Press, 2013

Simulate a zombie movie!

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Effective war on zombies

Introduce attacks on zombies at selected times T_0, T_1, \ldots, T_m .

Model: Replace α by

$$\alpha_0 + \omega(t)$$
,

where α_0 is constant and $\omega(t)$ is a series of Gaussian functions (peaks) in time:

$$\omega(t) = a \sum_{i=0}^{m} \exp\left(-\frac{1}{2}\left(\frac{t - T_i}{\sigma}\right)\right)$$

Must experiment with values of a (strength), σ (duration is 6σ), point of attacks (T_i) - with proper values humans beat the zombies!

Summary

- A complex spreading of diseases can be modeled by intuitive, simple accounting of movement between categories
- Such models are knowns as compartment models
- Result: difference equations that are easy to simulate on a computer
- ullet (Can let $\Delta t
 ightarrow 0$ and get differential equations)
- Easy to add new effects (vaccination, campaigns, zombification)

All these slides and associated programs are available

Site: https://github.com/hplgit/disease-modeling. Just do git clone https://github.com/hplgit/disease-modeling.git