Modeling the Spreading of Diseases

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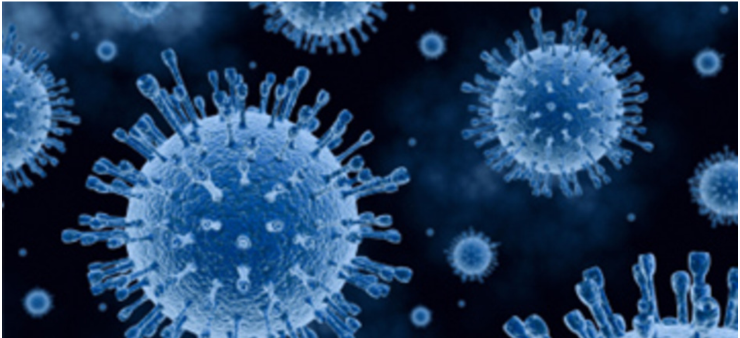
Aug 25, 2014



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

Assumptions:

- We have a perfectly mixed population in a confined area
- We do not consider spatial movements, just how the disease evolves in time
- 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, ...

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We keep track of 3 categories

Categories (SIR model):

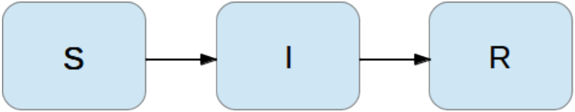
- **S**: susceptibles - who can get the disease
- **I**: infected - who have developed the disease and infect susceptibles
- **R**: recovered - who have recovered and become immune

Mathematical quantities:

$S(t)$, $I(t)$, $R(t)$ (no of people).

Goal:

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



The traditional modeling approach is very mathematical

- 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), properties, etc.
- Very few extensions of the model

$\Delta t\, \beta SI$ people move from S to I in a time inverval Δt

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.

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

Loss in $S(t)$:

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

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:

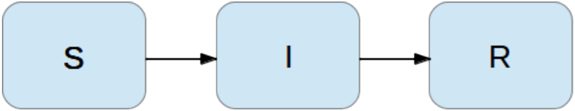
$$I(t+\Delta t) = I(t) + \Delta t\,\beta S(t)I(t) - \Delta t\,\nu I(t)$$

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

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

We have three equations for S, I, and R

$$S(t + \Delta t) = S(t) - \Delta t\, \beta S(t) I(t) \tag{1}$$
$$I(t + \Delta t) = I(t) + \Delta t\, \beta S(t) I(t) - \Delta t \nu I(t) \tag{2}$$
$$R(t + \Delta t) = R(t) + \Delta t\, \nu R(t) \tag{3}$$



Before we can compute with these, we must

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

The computation involves just simple arithmetics

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

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

- 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...

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R(2\Delta t) &= R(\Delta t) + \Delta t\, \nu R(\Delta t) \approx 0.00167
\end{aligned}
$$

Repeat...

$$
\begin{aligned}
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 R(2\Delta t) \approx 0.0025
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But this is getting boring! Let's ask a computer to do the work!

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First, some handy notation

$S^n = S(n\Delta t)$, $I^n = I(n\Delta t)$, $R^n = R(n\Delta t)$.
The equations can now be written as

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

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

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

With variables, arrays, and a loop we can program

Suppose we want to compute until $t = N\Delta t$, i.e., for $n = 0, 1, \ldots, N-1$. We can store $S^0, S^1, S^2, \ldots, S^N$ 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

Let time be measured in hours.

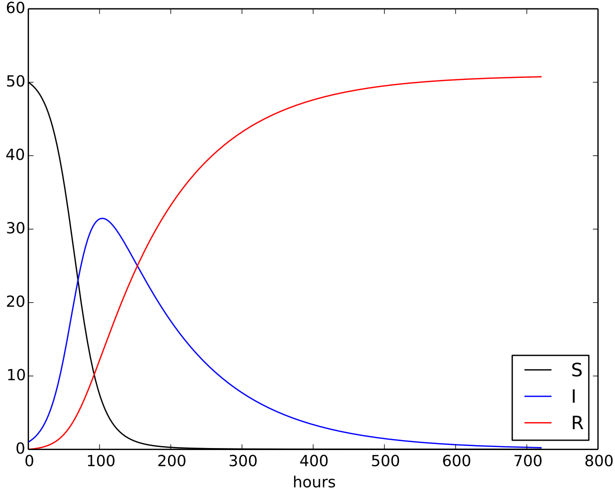
```
beta = 0.0013
nu =0.8333
dt = 0.1                # 6 min
D = 30                  # simulate for D days
N = int(D*24/dt)        # corresponding no of hours

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

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\begin{aligned}
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 R(t)
\end{aligned}
$$

The mathematician will now make a *differential equations*. First, divide by Δt and move S, I, and R to the left-hand side:

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

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

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

$$\begin{aligned} S'(t) &= -\beta S(t) I(t) \\ I'(t) &= \beta t S(t) I(t) - \nu I(t) \\ R'(t) &= \nu R(t) \end{aligned}$$

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.,

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

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)
- β must in some way be measured, but we don't know what it means...

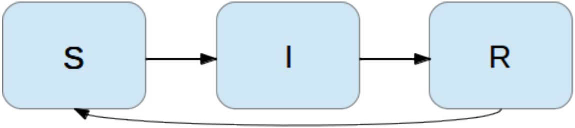
So what if we don't know β?

- Can still learn about the *dynamics* of diseases
- Can find the sensitivity to and influence of β
- Can apply *parameter estimation* procedures to fit β 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. ($1/\gamma$ is the mean time for immunity.)



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

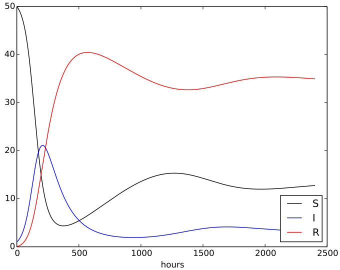
$$I^{n+1} = I^n + \Delta t\,\beta S^n I^n - \Delta t\,\nu I^n \tag{8}$$

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

No complications in the computational model!

The effect of loss of immunity

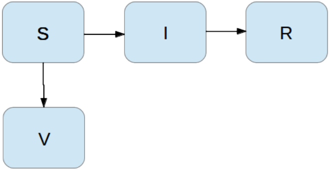
$1/\gamma = 50$ days. β reduced by 2 and 4:



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, $p\Delta t S$ will move to a vaccinated category, V. This does not affect the I and R categories.



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

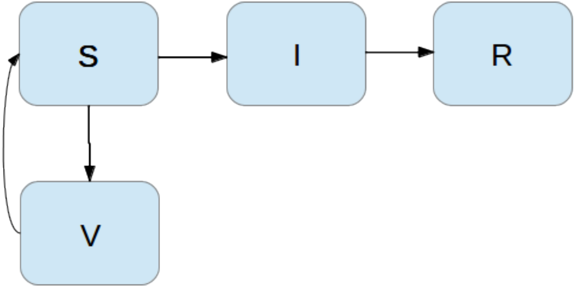
$$V^{n+1} = V^n + p\Delta t S^n \tag{11}$$

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

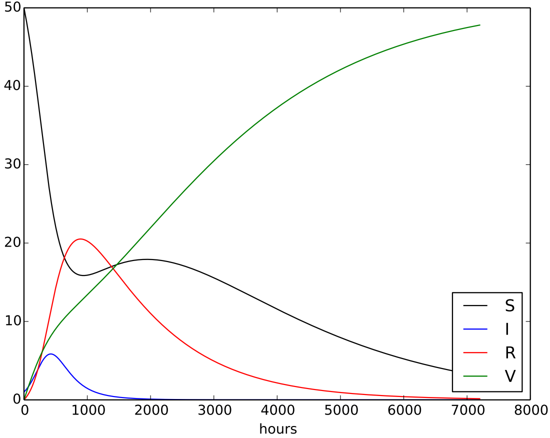
$$R^{n+1} = R^n + \Delta t\,\nu R^n - \Delta t\,\gamma R^n \tag{13}$$

Many possibilities for adjusting the model...

The effect of vaccination decreases, so we may move people back to the S category (term proportional to $\Delta t V$).



Effect of adding vaccination



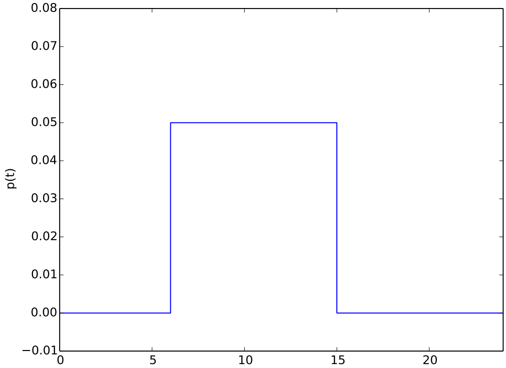
$(p = 0.005)$

What is the effect of an intensive vaccination campaign?

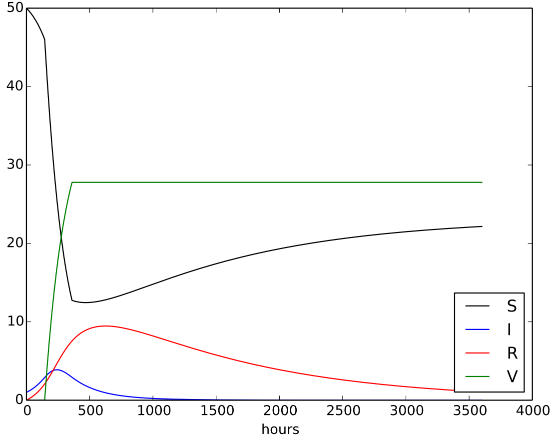
10 times more intense vaccination for 10 days, 6 days after outbreak:

$$p(t) = \begin{cases} 0.05, & 6 \leq t \leq 15, \\ 0, & \text{otherwise} \end{cases}$$

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



Could now let the computer run a lot of cases and find the optimal vaccination period.

We can experiment with other campaigns

Masks lower β:

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

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.

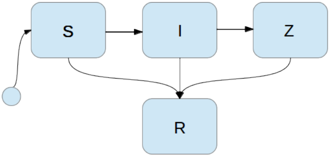
Zombie modeling is almost the same as SIR modeling

Categories.

1. S: susceptible humans who can become zombies
2. I: infected humans, being bitten by zombies
3. Z: zombies
4. 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

Dynamics of the zombie SIZR model



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

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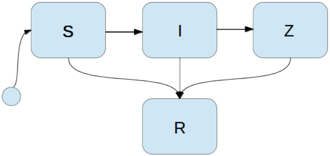

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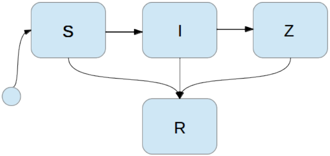

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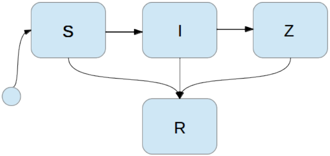

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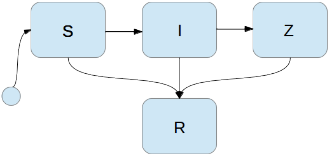

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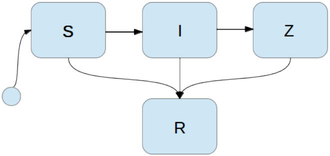

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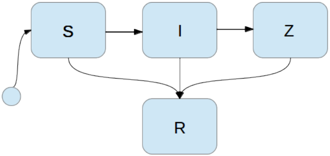
Dynamics of the zombie SIZR model



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

The four equations in the SIZR model for zombification

$$
\begin{aligned}
S^{n+1} &= S^n + \Delta t\,\Sigma - \Delta t\,\beta S^n Z - \Delta t\,\delta_S S^n \\
I^{n+1} &= I^n + \Delta t\,\beta S^n Z^n - \Delta t\,\rho I^n - \Delta t\,\delta_I I^n \\
Z^{n+1} &= Z^n + \Delta t\,\rho I^n - \Delta t\,\alpha S^n Z^n \\
R^{n+1} &= R^n + \Delta t\,\delta_S S^n + \Delta t\,\delta_I I^n + \Delta t\,\alpha S^n Z^n
\end{aligned}
$$

Interpretation of parameters:

- 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.

Simulate a zombie movie!

Three fundamental phases.

1. The initial phase (4 h)
2. The hysteric phase (24 h)
3. 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 and 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

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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)

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
- (Can let $\Delta t \rightarrow 0$ 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
```