MODELING EPIDEMICS 2022

COURSE AND ASSIGNMENT FINAL PRESENTATION

MICHELE BENEDETTI – VR488172 – UNIVERSITÁ DEGLI STUDI DI VERONA

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Epidemic Models

SIR Model

- First derived in 1927 by ***Kermack*** and ***McKendrick***, it is one of the most common models in epidemiology. It serves as a basis for more complex models and it is capable, in certain formulations, of accounting for contagion phenomena.

- It assumes the population to be split into 3 groups:
  - Susceptible population s (assumed to have no immunity to the disease)
  - Infected population i (assumed to have the disease)
  - Removed population r (assumed to have immunity to the disease)

- The change of s in time is the rate at which susceptible persons are infected, and the infected compartment i must also change, accordingly:

$$\begin{cases} \dfrac{ds}{dt} = -\dfrac{\beta}{n} si \\ \dfrac{di}{dt} = \dfrac{\beta}{n} si - \gamma i \\ \dfrac{dr}{dt} = \gamma i \end{cases}$$

where $n = s + i + r$ is the *total population,* β is the contact rate and γ the recovery rate

Force of Infection

- The term $\eta(t) = \frac{\beta}{n} i$ is called the ***Force of Infection*** and has unit $\left[\frac{1}{time}\right]$
- It is an epidemiological choice and not a mathematical one (in some cases it is taken to be a constant function)
- It is often useful to think of η as consisting of multiple parts:

$$\eta = Number\ of\ contacts\ per\ time \times Probability\ of\ transmission\ per\ infected\ contact \times Probability\ that\ the\ contact\ is\ infected$$

- Using this definition we can verify that our choice $\eta(t) = \frac{\beta}{n} i$ is coherent with the units (the term $\frac{i}{n}$ is the percentage of contacts that are infected)
- The contact rate β is often empirically estimated in models where number of contacts and transmission probabilities are well known

Herd Immunity Fraction

- Analyzing the SIR model we note that $\frac{\beta}{\gamma}\frac{s}{n} > 1 \Longrightarrow \frac{di}{dt} > 0$ and we therefore expect the infected population to increase
- This also implies $\frac{s}{n} > \frac{\gamma}{\beta} =: \widetilde{S_c}$ which we call the ***Herd Immunity Fraction*** of the susceptible population
- For given recovery and contact rates, the fraction of the susceptible population must be larger than $\widetilde{S_c}$ for the epidemic to spread in a sustained manner
- This implies that in order for the epidemic to die down we must have:

$$\frac{s}{n} < \widetilde{S_c} \Leftrightarrow \frac{r}{n} > 1 - \widetilde{S_c}$$

- This means that the *suceptible fraction* must be *less* than $\widetilde{S_c}$ or, equivalently, that the *removed fraction* must be *greater* than $1 - \widetilde{S_c}$
- More generally, the *population fraction with immunity* must be *at least* $1 - \widetilde{S_c}$

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Models for Sexually Transmitted Diseases

Compartmental Models

- The SIR Model belongs to the class of ***Compartmental Models***, in which the total quantities characterizing the system of interest are decomposed into 2 or more homogeneous units called compartments
- These models are ubiubiquitous all over the applied sciences: aside from biology, they are extensively used in chemistry, engineering, demography and in the social sciences

- Some examples of compartmental models in the applied sciences are:
  - Migration Models in demography
  - Predator-Prey Models and Competing Species Models in the social sciences
  - Reaction Models in chemistry
  - Phase Models in metallurgy

- This framework can be applied to far more complex models. Let us for example think about a common sexually transmitted disease: **HIV**

Generic HIV Model - Assumptions

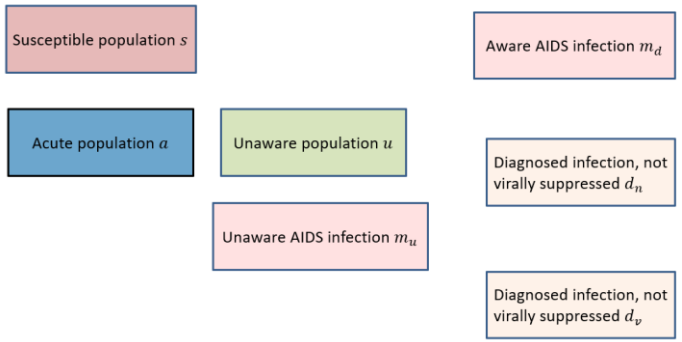
- In order to build a model capable of correctly describing and predicting the behaviour of this disease, we first have to think about the facts that we already know about the disease itself
- HIV diagnosis can occur many years after infection and many people may not be aware of their infection
- The rate at which people transmit HIV depends heavily on their awareness and treatment status

- Someone may be:
  - Acutely infected
  - Non acutely infected, unaware of infection
  - AIDS, unaware of infection
  - Aware of infection, not virally suppressed
  - Aware of infection, virally suppressed

- When someone is virally suppressed their probability of transmitting the disease is essentially 0, but people (for various reasons) may not adhere perfectly to their treatment and lose viral suppression

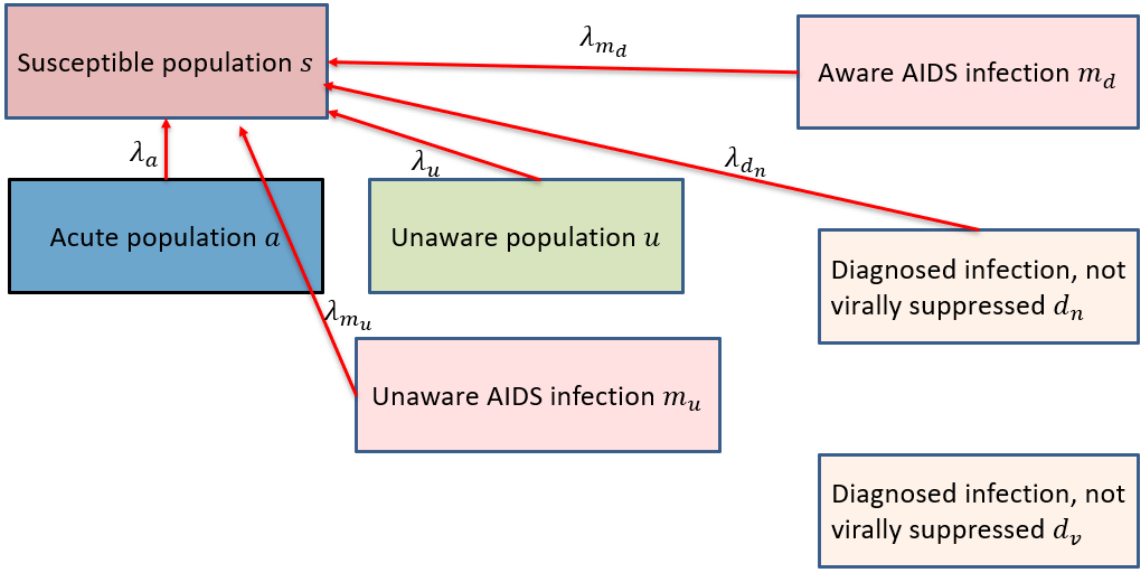
Generic HIV Model - Graphs

- The last and fundamental fact known about HIV is that nobody recovers from it: it is a lifelong condition
- Given this knowledge, it appears that the SIR model framework might not be suitable to describe this situation
- Indeed, in general, the infected population is not homogeneous as different groups mix and transmit at different rates. This prevents us from treating them all as «infected», since this wouldn't make any sense
- Moreover, nobody recovers from the condition and removal only occurs at death
- Finally, we need to account for dynamics which were not considered in the SIR model, like treatment adherence
- We can still use the compartmental framework to build a suitable model, and a way of doing this is to use graphs to visualize things a little bit better:



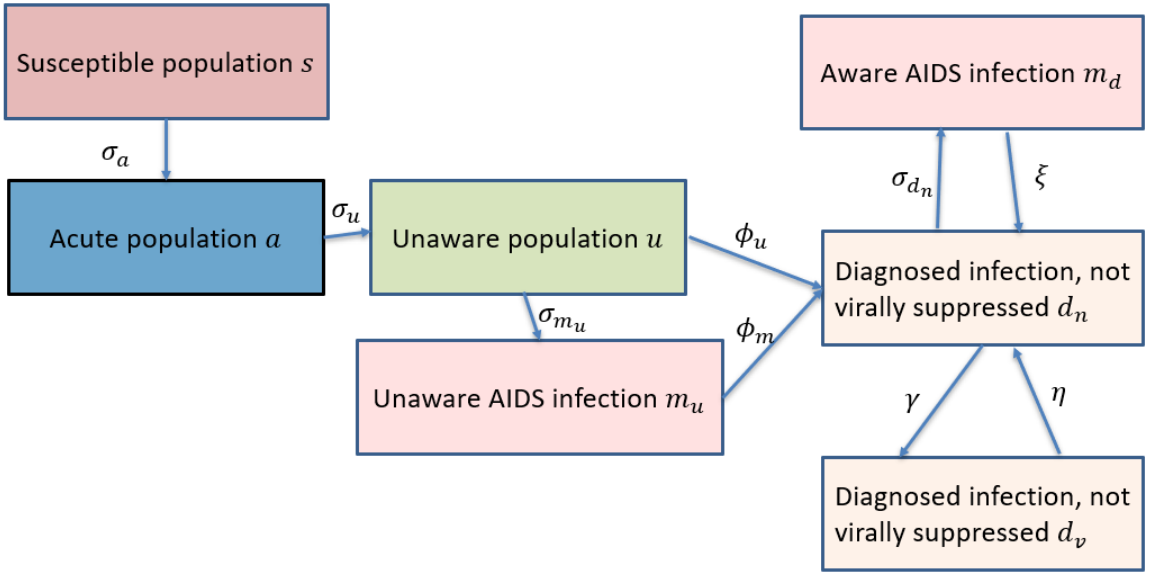
Incidence Functions

- The ***Incidence Functions*** (i.e. the functions which are always proportional to the vulnerable population) must then be inserted:



Contact Rates

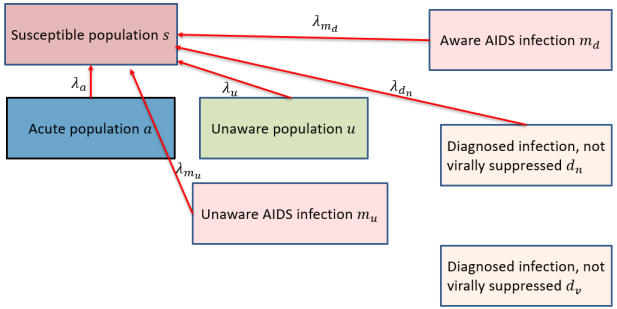
- Now, we can also insert the various contact rates and treatment adherence parameters:

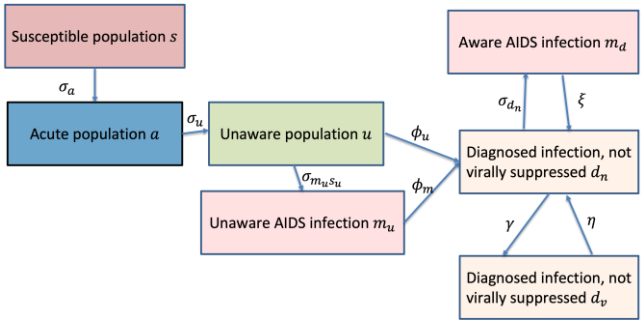


ODE System

- Eventually, our Generic HIV Model reads as follows:

$$
\begin{aligned}
\dot{s} &= -\left(\lambda_a + \lambda_u + \lambda_{m_u} + \lambda_{d_n} + \lambda_{m_d}\right)s - \mu_s s \\
\dot{a} &= \left(\lambda_a + \lambda_u + \lambda_{m_u} + \lambda_{d_n} + \lambda_{m_d}\right)s - \sigma_u a - \mu_a a \\
\dot{u} &= \sigma_u a - \sigma_{m_u} u - \phi_u u - \mu_u u \\
\dot{m}_u &= \sigma_{m_u} u - \phi_m m_u - \mu_{m_u} m_u \\
\dot{d}_n &= \phi_u u + \phi_m m_u + \xi m_d + \eta d_v - \sigma_{d_n} d_n - \gamma d_n - \mu_{d_n} d_n \\
\dot{d}_v &= \gamma d_n - \eta d_v - \mu_{d_v} d_v \\
\dot{m}_d &= \sigma_{d_n} d_n - \xi m_d - \mu_{m_d} m_d
\end{aligned}
$$





Model for a generic STD - Assumptions

- We now want to construct a model for an hypothetical Sexually Transmitted Disease (STD), using the following assumptions

- We consider 3 groups, each one with their own contact rates:
  - ***MSM*** (men who have sex with men) have an average of 5.1 sexual partners per year and 16 sexual contacts per partner, 84.4% of whom are MSM and 15.2% of whom are HetF
  - ***HetF*** (heterosexual females) have an average of 1.4 sexual partners per year and 37 sexual contacts per partner, 4% of whom are MSM and 96% of whom are HetM
  - ***HetM*** (heterosexual men) have an average of 1.8 sexual partners per year and 23 sexual contacts per partner, 100% of whom are HetF

- Persons can either be ***diagnosed*** or ***undiagnosed***
- Disease is identified through a test, and the 3 groups test at rates $\Phi_{MSM}, \Phi_{HetF}, \Phi_{HetM}$ respectively
- Diagnosed individuals are assumed to be on treatment and are assumed to take precautions that reduce the probability of transmission by 98%
- The condition is lifelong and does not go away. Undiagnosed individuals die at 2.5 times the rate of the general population while diagnosed individuals on treatment have the same mortality rates ($\mu_{MSM}, \mu_{HetF}, \mu_{HetM}$) as the general population

Force of Infection Terms

- We now want to write the full expressions for the Force of Infection terms $\lambda_{MSM}, \lambda_{HetF}, \lambda_{HetM}$. Probabilities of transmission through a single contact are denoted as follows:
  - Male to Female: $p_{M\to F}$
  - Female to Male: $p_{F\to M}$
  - Male to Male: $p_{M\to M}$
- We assume exponential distribution for all the infection rates. Denoting the *Infected Diagnosed* and the *Infected Undiagnosed* populations with the subscripts ***u*** and ***d*** respectively, we have the following:

$$\lambda_{MSM_u} = -\frac{MSM_u}{MSM+MSM_u+MSM_d}[5.1\cdot 16\cdot 0.848\cdot \log(1-p_{M\to M}) + 1.4\cdot 37\cdot 0.04\cdot \log(1-p_{M\to F})]$$

$$\lambda_{MSM_d} = -\frac{MSM_d}{MSM+MSM_u+MSM_d}[5.1\cdot 16\cdot 0.848\cdot \log(1-0.02\cdot p_{M\to M}) + 1.4\cdot 37\cdot 0.04\cdot \log(1-0.02\cdot p_{M\to F})]$$

$$\lambda_{HetF_u} = -\frac{HetF_u}{HetF+HetF_u+HetF_d}[5.1\cdot 16\cdot 0.152\cdot \log(1-p_{F\to M}) + 1.8\cdot 23\cdot \log(1-p_{F\to M})]$$

$$\lambda_{HetF_d} = -\frac{HetF}{HetF+HetF_u+HetF_d}[5.1\cdot 16\cdot 0.152\cdot \log(1-0.02\cdot p_{F\to M}) + 1.8\cdot 23\cdot \log(1-0.02\cdot p_{F\to M})]$$

$$\lambda_{HetM_u} = -\frac{HetM_u}{HetM+HetM_u+HetM_d}[1.4\cdot 37\cdot 0.96\cdot \log(1-p_{M\to F})]$$

$$\lambda_{HetM_d} = -\frac{HetM_d}{HetM+HetM_u+HetM_d}[1.4\cdot 37\cdot 0.96\cdot \log(1-0.02\cdot p_{M\to F})]$$

ODE System

- The Force of Infection terms are then defined as follows:

$$\lambda_{MSM} = \lambda_{MSM_u} + \lambda_{MSM_d}$$
$$\lambda_{HetF} = \lambda_{HetF_u} + \lambda_{HetF_d}$$
$$\lambda_{HetM} = \lambda_{HetM_u} + \lambda_{HetM_d}$$

- We can now write the full ODE system:

$$\dot{MSM} = -(\lambda_{MSM} + \lambda_{HetF}) \cdot MSM - \mu_{MSM} \cdot MSM$$
$$\dot{HetF} = -(\lambda_{MSM} + \lambda_{HetM}) \cdot HetF - \mu_{HetF} \cdot HetF$$
$$\dot{HetM} = -\lambda_{HetF} \cdot HetM - \mu_{HetM} \cdot HetM$$
$$\dot{MSM_u} = (\lambda_{MSM} + \lambda_{HetF}) \cdot MSM - \Phi_{MSM} \cdot MSM_u - 2.5 \cdot \mu_{MSM} \cdot MSM_u$$
$$\dot{HetF_u} = (\lambda_{MSM} + \lambda_{HetM}) \cdot HetF - \Phi_{HetF} \cdot HetF_u - 2.5 \cdot \mu_{HetF} \cdot HetF_u$$
$$\dot{HetM_u} = \lambda_{HetF} \cdot HetM - \Phi_{HetM} \cdot HetM_u - 2.5 \cdot \mu_{HetM} \cdot HetM_u$$
$$\dot{MSM_d} = \Phi_{MSM} \cdot MSM_u - \mu_{MSM} \cdot MSM_d$$
$$\dot{HetF_d} = \Phi_{HetF} \cdot HetF_u - \mu_{HetF} \cdot HetF_d$$
$$\dot{HetM_d} = \Phi_{HetM} \cdot HetM_u - \mu_{HetM} \cdot HetM_d$$

Test and Mortality Rates

- The probability that MSM, HetF and HetM take a test each month are 25%, 5% and 1% respectively, while the probability that MSM, HetF and HetM die in a year are 0.8%, 0.25% and 0.4% respectively
- Based on these assumptions we now want to find the test rates and the mortality rates for each group
- Recall the cumulative distribution function for the exponential distribution:

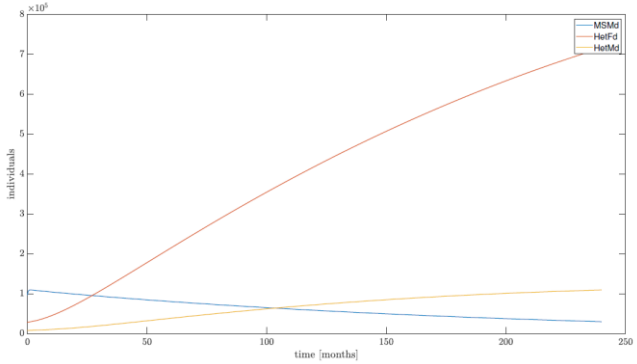
$$P(t,\gamma) = 1 - e^{-\gamma t} \Longrightarrow \gamma = -\frac{\log(1-p)}{t}$$

- In order to be consistent with the time units, we consider the probability of taking a test each month referred to one month and the probability to die referred to one year:

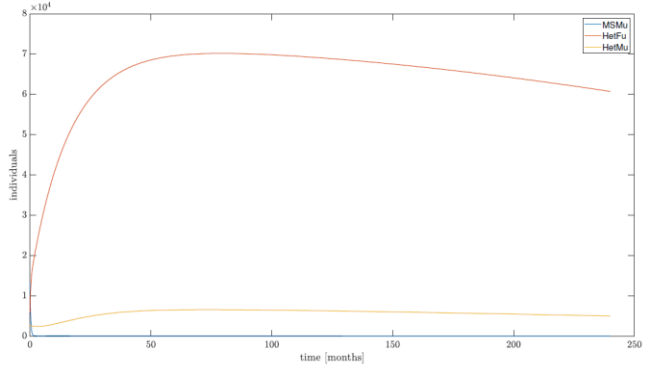
$$\begin{aligned}
\Phi_{MSM} &= -12 \cdot \log(1 - p_{MSM}) \\
\Phi_{HetF} &= -12 \cdot \log(1 - p_{HetF}) \\
\Phi_{HetM} &= -12 \cdot \log(1 - p_{HetM}) \\
\mu_{MSM} &= -\log(1 - q_{MSM}) \\
\mu_{HetF} &= -\log(1 - q_{HetF}) \\
\mu_{HetM} &= -\log(1 - q_{HetM})
\end{aligned}$$

where $p_{MSM} = 25\%,\ p_{HetF} = 5\%,\ p_{HetM} = 1\%,\ q_{MSM} = 0.8\%,\ q_{HetF} = 0.25\%,\ q_{HetM} = 0.4\%$

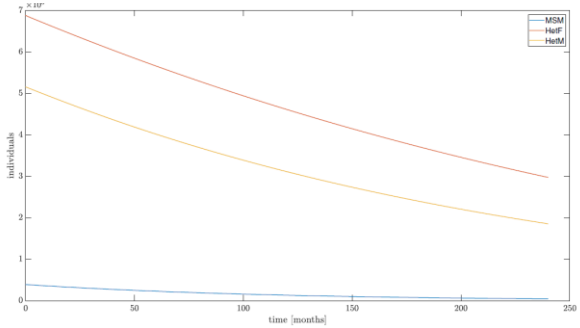
Model for a generic STD - Results



Infected diagnosed population



Infected undiagnosed population



Susceptible population

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Spatial Information

Spatial Compartments

The simplest and most natural way to extend the previous models into space is via the addition of spatially-designated compartments. This can be seen as coupling multiple SIR-type models together

PDE

It overcomes the limitations of the spatial compartments approach by representing a truly space-continuous dynamics. This comes, however, with much greater expense of resources for the numerical simulations

Spatial Compartments

- This is a very natural and computationally inexpensive way to model spatial variation
- Theoretically, one could add arbitrarily many spatial compartments
- However, as we'll se later, this approach is ultimately limited in its ability to describe spatial dynamics, since it is not able to represent true space-continuous dynamics
- We want to model (using the SIR Model as the basic structure) a situation in which we have 2 regions (Milano and Codogno) each with its own characteristics:

$$s_c, i_c, r_c, s_m, i_m, r_m$$

- At the beginning of the outbreak we have some infections in Codogno only:

$$i_c(0) > 0, i_m(0) = 0$$

- Since some Codogno citizens work in Milano, we assume that there is contact (hence transmission) between Codogno and Milano

2-Region SIR Model – ODE System

- Following these assumptions, the full ODE system reads as follows:

$$\frac{ds_m}{dt} = -\frac{\beta_{cm}}{N_c} s_m i_c - \frac{\beta_{mm}}{N_m} s_m i_m$$
$$\frac{di_m}{dt} = \frac{\beta_{cm}}{N_c} s_m i_c + \frac{\beta_{mm}}{N_m} s_m i_m - \gamma i_m$$
$$\frac{dr_m}{dt} = \gamma i_m$$
$$\frac{ds_c}{dt} = -\frac{\beta_{mc}}{N_m} s_c i_m - \frac{\beta_{cc}}{N_c} s_c i_c$$
$$\frac{di_c}{dt} = \frac{\beta_{mc}}{N_m} s_c i_m + \frac{\beta_{cc}}{N_c} s_c i_c - \gamma i_c$$
$$\frac{dr_c}{dt} = \gamma i_c$$

where γ is the *removal rate* and β_{ij} is the rate at which an individual in compartment i produces infections in compartments j

2-Region SIR Model - DDF

- In order to simplify the notation we take the following substitutions:

$$\frac{\beta_{cm}}{N_c} = \gamma_{cm},\ \frac{\beta_{mm}}{N_m} = \gamma_{mm},\ \frac{\beta_{mc}}{N_m} = \gamma_{mc},\ \frac{\beta_{cc}}{N_c} = \gamma_{cc},\ \gamma = \alpha$$

- We then obtain the so-called *density dependent* formulation of the model:

$$\begin{aligned}
\frac{ds_m}{dt} &= -\gamma_{cm} s_m i_c - \gamma_{mm} s_m i_m \\
\frac{di_m}{dt} &= \gamma_{cm} s_m i_c + \gamma_{mm} s_m i_m - \alpha i_m \\
\frac{dr_m}{dt} &= \alpha i_m \\
\frac{ds_c}{dt} &= -\gamma_{mc} s_c i_m - \gamma_{cc} s_c i_c \\
\frac{di_c}{dt} &= \gamma_{mc} s_c i_m + \gamma_{cc} s_c i_c - \alpha i_c \\
\frac{dr_c}{dt} &= \alpha i_c
\end{aligned}$$

2-Region SIR Model – Contact Rates

- We assume the population of Milano and Codogno to be 2e6 and 5e5 respectively. Moreover, the initial infected pool is 500 in Codogno and 0 (as seen before) in Milano. The removal rate is $\gamma = \alpha = \frac{1}{18}$
- The probability of transmission in a close contact is 1.2e-2, while in a light contact it is 5.3e-4
- People in Milano have an average of 42 light contacts and 6.1 close contacts per day with other Milano inhabitants, and 3.06e-2 light contacts and 9.1e-3 close contacts per day with people from Codogno
- People in Codogno have an average of 18 light contacts and 3.8 close contacts per day with other Codogno inhabitants, and 5.1 light contacts and 1.51 close contacts per day with people from Milano
- As we did before, we assume all the probabilities to be exponentially distributed, so we have the following expressions for the contact rates:

$$\beta_{cm} = -5.1 \cdot \log(1 - 0.00053) - 1.51 \cdot \log(1 - 0.012) \Longrightarrow \gamma_{cm} = \frac{\beta_{cm}}{12000}$$

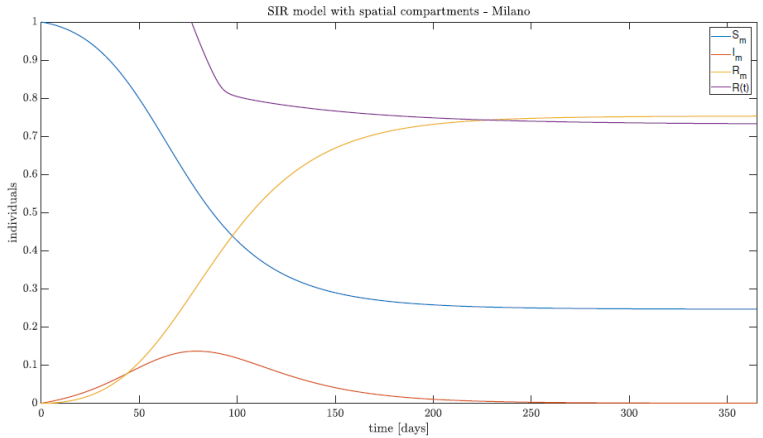
$$\beta_{mm} = -42 \cdot \log(1 - 0.00053) - 6.1 \cdot \log(1 - 0.012) \Longrightarrow \gamma_{cm} = \frac{\beta_{mm}}{2000000}$$

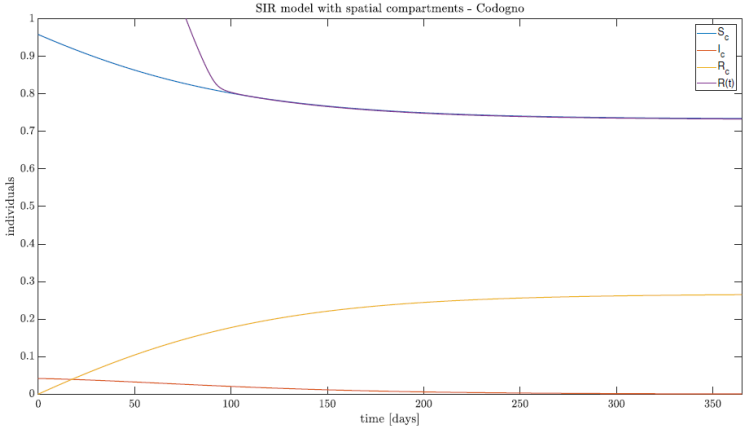
$$\beta_{mc} = -0.0306 \cdot \log(1 - 0.00053) - 0.0091 \cdot \log(1 - 0.012) \Longrightarrow \gamma_{cm} = \frac{\beta_{mc}}{2000000}$$

$$\beta_{cc} = -18 \cdot \log(1 - 0.00053) - 3.8 \cdot \log(1 - 0.012) \Longrightarrow \gamma_{cc} = \frac{\beta_{cc}}{12000}$$

2-Region SIR Model - Results

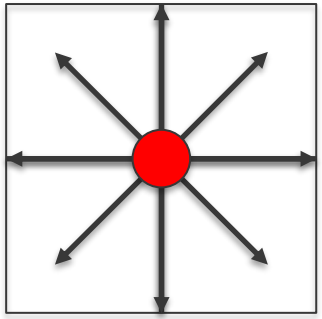
- With these parameter values, the following results are obtained:





Diffusion and Random Walks

- We would like to describe spatial variation at the macroscopic level (i.e. continuously)
- Assume any given infinitesimal particle to be able to move in one of 8 possible direction or stand still with equal probability
- At each new position the process repeats independently. This process is called a ***random walk*** and it operates at a microscopic scale:



- At the macroscopic scale, where the particles are represented as a continuum, this proces forms the basis of the ***diffusion*** pehomenon

Diffusion and Reaction

- The most common application of diffusion is the Heat Equation for the distribution of temperature $T(x,t)$ in a domain Ω:

$$\rho C_p \frac{\partial T}{\partial t} = \kappa \Delta T \text{ in } \Omega$$

- In a conservative form, assuming κ to be non-constant, we can write the above equation as follows:

$$\rho C_p \frac{\partial T}{\partial t} = \nabla \cdot (\kappa \nabla T) \text{ in } \Omega$$

- The terms in red are the ***diffusive terms***
- In our model, the diseased individuals represent the particles and the diffusion pehomenon represents the particle motion
- The «chemical reaction» is still similar to what we observed in the ODE models

Diffusion and Reaction - PDE System

- We now derive an SIR-like Model with spatial diffusion. We assume that new births enter the susceptible compartment at a rate β and that there is a generic (non disease) mortality rate μ:

$$\frac{\partial s}{\partial t} = \beta(s+i+r) - \gamma si + \nabla \cdot (\nu_s \nabla s) - \mu s \text{ in } \Omega$$
$$\frac{\partial i}{\partial t} = \gamma si - \alpha i + \nabla \cdot (\nu_i \nabla i) - \mu i \text{ in } \Omega$$
$$\frac{\partial r}{\partial t} = \alpha i + \nabla \cdot (\nu_r \nabla r) - \mu r \text{ in } \Omega$$

  where the parameters ν are the diffusivity coefficients and $\Omega \subset \mathbb{R}^2$

- This model is obviously incomplete: we need boundary conditions. The most useful type of boundary conditions for our purposes are the ***Neumann Boundary Conditions***:

$$(\nabla s) \cdot \boldsymbol{n} = g \text{ on } \partial\Omega$$

  where $\boldsymbol{n}$ is the outward pointing unit normal on $\partial\Omega$ (properly understood as flux)

Diffusion and Reaction – BC

- The homogeneous Neumann boundary condition corresponds to complete isolation of the domain (zero flux: nobody enters or leaves):

$$(\nu_s \nabla s) \cdot \boldsymbol{n} = 0, (\nu_\mathrm{i} \nabla i) \cdot \boldsymbol{n} = 0, (\nu_r \nabla r) \cdot \boldsymbol{n} = 0 \text{ on } \partial\Omega$$

- If we wanted to model the influence of susceptible, infected and removed persons entering and leaving the domain at net flux rates g_s, g_i, g_r we would have written the following boundary conditions:

$$(\nu_s \nabla s) \cdot \boldsymbol{n} = g_s, (\nu_\mathrm{i} \nabla i) \cdot \boldsymbol{n} = g_i, (\nu_r \nabla r) \cdot \boldsymbol{n} = g_r \text{ on } \partial\Omega$$

- Adding the 3 equations together and assuming that we have $\nu = \nu_s = \nu_i = \nu_r$, we obtain the following formulation:

$$\frac{\partial n}{\partial t} = \nabla \cdot (\nu \nabla n) + (\beta - \mu) n$$

where $n = s + i + r$

Continuum Mechanics Framework

- Such models have a natural interpretation in terms of conservation laws and balance of forces, therefore we can understand them in terms of familiar concepts from Continuum Mechanics
- Consider the following generic continuum mechanics equation:

$$\partial_t \boldsymbol{u} - \nabla \cdot \boldsymbol{F} + \boldsymbol{b} = \boldsymbol{0} \quad (1)$$
$$\boldsymbol{\varepsilon} = \nabla \boldsymbol{u} \quad (2)$$
$$\boldsymbol{F} = \boldsymbol{F}(\boldsymbol{u}, \boldsymbol{\varepsilon}) \quad (3)$$
$$\boldsymbol{b} = \boldsymbol{b}(\boldsymbol{u}) \quad (4)$$

Where:

- (1) is an *internal force balance* in terms of an internal force $\boldsymbol{F}$ which is thermodynamically conjugate to $\boldsymbol{u}$
- (2) is the *compatibility relation*
- (3) is the *constitutive relation:* it defines the relation between compatibility and balance equations
- (4) is the *loading relation:* it depends algebraically on the unknown terms, describing the interaction between compartments

COVID-19 Model - Assumptions

- We now build a generic COVID-19 model using the continuum mechanics framework as a basis and the following assumptions:

    1. Movement is proportional to population size
    2. No movement occurs among the deceased population
    3. There is a latency period between exposure and development of symptoms
    4. The probability of contagion increases with population size
    5. Some portion of the exposed population never develop symptoms (*asymptomatic patients)*
    6. Both symptomatic and asymptomatic patients are capable of spreading the disease
    7. All living persons are capable of reproduction (no age-structuring)
    8. The non-COVID-19 mortality rate is independent of population compartment
    9. New births are susceptible to the virus

- We now use these assumptions to derive the model, starting with the constitutive relation

Contstitutive Relation

- Because of assumption 1, movement is proportional to the population size. We set $n = s + e + i + r$ as the living population and define the constitutive relation as follows:

$$\boldsymbol{F}(\boldsymbol{u}, \boldsymbol{\varepsilon}) = n\, \boldsymbol{E}\boldsymbol{\varepsilon},$$

$$\boldsymbol{E} = \begin{bmatrix} \bar{\nu}_s & 0 & 0 & 0 & 0 \\ 0 & \bar{\nu}_e & 0 & 0 & 0 \\ 0 & 0 & \bar{\nu}_i & 0 & 0 \\ 0 & 0 & 0 & \bar{\nu}_r & 0 \\ 0 & 0 & 0 & 0 & 0 \end{bmatrix}$$

- Recall that by equation (2) we have $\boldsymbol{\varepsilon} = \boldsymbol{\nabla}\mathbf{u}$
- The ν have unit $[L^2T^{-1}P^{-1}]$ where L, T, P are characteristic length, time and population scales, respectively
- The element $\boldsymbol{E}(5,5)$ is 0 as a result of assumption 2 (deceased people do not move)

Loading Relation

- We now define the loading relation described by the vector $\boldsymbol{b} = \boldsymbol{b}(\boldsymbol{u})$, which defines interaction between compartments
- By assumption 3, there is a latency period before development of symptoms. All patients exposed to the virus first move from the susceptible compartment into the exposed compartment:

$$\partial_t e \propto -\partial_t s$$

- By assumption 6 each exposed individual could become infected (symptomatic) or exposed and asymptomatic:

$$\partial_t s \propto -\gamma_e(e,n)s \; -\gamma_i(i,n)s$$
$$\partial_t e \propto \gamma_e(e,n)s + \gamma_i(i,n)s$$

- Assume also that the contact rates γ_e, γ_i are linear in e and i with unit $[T^{-1}P^{-1}]$

Loading Relation (continued)

- Dependence on n is given through a *depensation effect* or *Allee term* A (unit $[P]$):

$$\partial_t s \propto -\left(1-\frac{\bar{A}}{n}\right)\bar{\gamma}_e\, es \; -\left(1-\frac{\bar{A}}{n}\right)\bar{\gamma}_i si$$

$$\partial_t e \propto \left(1-\frac{\bar{A}}{n}\right)\bar{\gamma}_e es + \left(1-\frac{\bar{A}}{n}\right)\bar{\gamma}_i si$$

  - When n is large the effect of this term is small, consistently with assumption 4
  - This parameter must be carefully chosen as it can accurately capture severe contagion in urban areas and mild contagion in rural ones

Loading Relation (continued)

- By assumption 3 there is a latency period before the development of the symptoms: all patients exposed to the virus first move from the susceptible compartment into the infected compartment after a period of time $\bar{\sigma}$:

$$\partial_t i \propto \bar{\sigma} e$$
$$\partial_t e \propto -\bar{\sigma} e$$

- Assumption 5, however, states that some patients will be asymptomatic and never enter the infected compartment, moving instead to the recovered compartment after a period of time $\bar{\alpha}_e$:

$$\partial_t e \propto -\bar{\alpha}_e e$$
$$\partial_t r \propto \bar{\alpha}_e e$$

- Both $\bar{\sigma}$ and $\bar{\alpha}_e$ have unit $[T^{-1}]$

Loading Relation (continued)

- Some portion of the infected population will move into the recovered compartment:

$$\partial_t i \propto -\bar{\alpha}_r i$$
$$\partial_t r \propto \bar{\alpha}_r i$$

- Meanwhile, some portion of the infected patients will die, entering the deceased compartment (this ***only*** considers COVID-19 deaths):

$$\partial_t i \propto -\bar{\phi}_d i$$
$$\partial_t d \propto \bar{\phi}_d i$$

- Assumption 7 implies that compartment s grows proportionally to total population n with a reproduction rate $\bar{\beta}$ (unit $[T^{-1}]$)
- Assumption 9 implies that these new births go to the susceptible compartment
- Assumption 8 implies that all compartments have a non-COVID-19 mortality rate $\bar{\mu}$ (unit $[T^{-1}]$)

COVID-19 Model - PDE System

- The complete COVID-19 model reads as follows:

$$\partial_t s = \bar{\beta} n - \left(1 - \frac{\bar{A}}{n}\right) \bar{\gamma}_e \, es - \left(1 - \frac{\bar{A}}{n}\right) \bar{\gamma}_i si - \bar{\mu} s + \nabla \cdot (n \, \nu_s \nabla s)$$

$$\partial_t e = \left(1 - \frac{\bar{A}}{n}\right) \bar{\gamma}_e \, es + \left(1 - \frac{\bar{A}}{n}\right) \bar{\gamma}_i si - \bar{\alpha}_e e - \bar{\sigma} e - \bar{\mu} e + \nabla \cdot (n \, \nu_e \nabla e)$$

$$\partial_t i = e - \bar{\phi}_d i - \bar{\alpha}_r i - \bar{\mu} i + \nabla \cdot (n \, \nu_i \nabla i)$$

$$\partial_t r = \bar{\alpha}_e e + \bar{\alpha}_r i - \bar{\mu} r + \nabla \cdot (n \, \nu_r \nabla i)$$

$$\partial_t d = \bar{\phi}_d i$$

- Written in the continuum mechanics notation, the loading relation term becomes:

$$\boldsymbol{B}(\boldsymbol{u}) = \begin{bmatrix} \bar{\mu} - \bar{\beta} & \left(1 - \frac{\bar{A}}{n}\right) \bar{\gamma}_e s - \bar{\beta} & \left(1 - \frac{\bar{A}}{n}\right) \bar{\gamma}_i s - \bar{\beta} & \bar{\beta} & 0 \\ 0 & \mu - \left(1 - \frac{\bar{A}}{n}\right) \bar{\gamma}_e s + \bar{\sigma} + \bar{\alpha}_e & -\left(1 - \frac{\bar{A}}{n}\right) \bar{\gamma}_i s & 0 & 0 \\ 0 & -\bar{\sigma} & \bar{\mu} + \bar{\phi}_d + \bar{\alpha}_r & 0 & 0 \\ 0 & -\bar{\alpha}_e & -\bar{\alpha}_r & \bar{\mu} & 0 \\ 0 & 0 & -\bar{\phi}_d & 0 & 0 \end{bmatrix}$$

Nonlinear Diffusion

- Adding all the terms together and assuming that all the diffusivity rates are equal we obtain:

$$\partial_t n \; - \nabla \cdot (\bar{\nu}\, n\, \nabla\, n) = \left(\bar{\beta} - \bar{\mu}\right) n - \bar{\phi}_d i$$

- This means that the whole model can be interpreted as a nonlinear continuity equation over the living population n
- Using the product rule we get:

$$\partial_t n \; - \nabla \cdot (\bar{\nu}\, n\, \nabla\, n) = \left(\bar{\beta} - \bar{\mu}\right) n - \bar{\phi}_d i$$
$$\partial_t n \; - \bar{\nu}\, n\, \Delta\, n - \nabla(\bar{\nu}\, n) \cdot \nabla\, n = \left(\bar{\beta} - \bar{\mu}\right) n - \bar{\phi}_d i$$

- The term highlighted in red shows that the nonlinear diffusion doesn't only act as a diffusion in the traditional sense, but it also has some characteristics of a convection phenomenon

4

Derivation of R_t

Derivation of R_t

- We want now to derivate an expression for the effective viral reproduction number R_t using the next-generation matrix method. We use the previous 2-region SIR Model (Milano – Codogno) written in the density dependent formulation:

$$\frac{ds_m}{dt} = -\gamma_{cm} s_m i_c - \gamma_{mm} s_m i_m$$
$$\frac{di_m}{dt} = \gamma_{cm} s_m i_c + \gamma_{mm} s_m i_m - \alpha i_m$$
$$\frac{dr_m}{dt} = \alpha i_m$$
$$\frac{ds_c}{dt} = -\gamma_{mc} s_c i_m - \gamma_{cc} s_c i_c$$
$$\frac{di_c}{dt} = \gamma_{mc} s_c i_m + \gamma_{cc} s_c i_c - \alpha i_c$$
$$\frac{dr_c}{dt} = \alpha i_c$$

Derivation of R_t (continued)

- The diseased portions of the population (i.e. anyone capable of spreading the disease) are identified by the infected compartments:

$$\begin{cases} \dfrac{di_m}{dt} = \gamma_{cm} s_m i_c + \gamma_{mm} s_m i_m - \alpha i_m \\ \dfrac{di_c}{dt} = \gamma_{mc} s_c i_m + \gamma_{cc} s_c i_c - \alpha i_c \end{cases}$$

- We can write the above equations like follows:

$$\frac{d}{dt}\begin{pmatrix} i_m \\ i_c \end{pmatrix} = \begin{pmatrix} \gamma_{mm} s_m - \alpha & \gamma_{cm} s_m \\ \gamma_{mc} s_c & \gamma_{cc} s_c - \alpha \end{pmatrix}\begin{pmatrix} i_m \\ i_c \end{pmatrix} = (N - V)\begin{pmatrix} i_m \\ i_c \end{pmatrix}$$

where:

$N \coloneqq \begin{pmatrix} \gamma_{mm} s_m & \gamma_{cm} s_m \\ \gamma_{mc} s_c & \gamma_{cc} s_c \end{pmatrix}$ is the matrix corresponding to ***new cases***,

$V \coloneqq \begin{pmatrix} \alpha & 0 \\ 0 & \alpha \end{pmatrix}$ is the matrix corresponding to ***existing cases***

Derivation of R_t (continued)

- We now compute the Next-Generation Matrix:

$$NV^{-1} = \begin{pmatrix} \gamma_{mm}s_m & \gamma_{cm}s_m \\ \gamma_{mc}s_c & \gamma_{cc}s_c \end{pmatrix} \cdot \begin{pmatrix} \frac{1}{\alpha} & 0 \\ 0 & \frac{1}{\alpha} \end{pmatrix} = \begin{pmatrix} \gamma_{mm}s_m \cdot \frac{1}{\alpha} & \gamma_{cm}s_m \cdot \frac{1}{\alpha} \\ \gamma_{mc}s_c \cdot \frac{1}{\alpha} & \gamma_{cc}s_c \cdot \frac{1}{\alpha} \end{pmatrix}$$

where we note that the element $NV^{-1}(i,j)$ corresponds to the average amount of infections at time t produced by an individual entering the $j-th$ infected compartment and spreading the infection into the $i-th$ city at rate β_{ji}

- Finally, R_t is defined as follows:

$$R_t \coloneqq \rho(NV^{-1}) = \max\{|\lambda| : \lambda \text{ eigenvalue of } NV^{-1}\}$$

which, in our case, leads to the following expression:

$$R_t = \frac{\gamma_{cc}s_c + \gamma_{mm}s_m + \sqrt{(\gamma_{cc}s_c)^2 + (\gamma_{mm}s_m)^2 - 2\gamma_{cc}s_c\gamma_{mm}s_m + 4\gamma_{cm}s_m\gamma_{mc}s_c}}{2\alpha}$$

THANK YOU
FOR YOUR ATTENTION