Comorbidity in epidemic spreading processes

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In this work, we study the spread of two pathogens in random world and scale-free networks by introducing a model that combines the SIS and the SIR models. The process proposed will infect the population with two different pathogens. Each of these in isolation follows a simple SIS dynamics. However they follow the SIR dynamics once comorbidity occurs and both pathogens are present in the same individual. We analyse how the endemic threshold λ_c is affected by the interaction between pathogens and how they spread over time.

I. INTRODUCTION

The most common models for studying epidemic models are Susceptible-Infected-Susceptible (SIS) and Susceptible-Infected-Remove (SIR) model. The SIS model describes an infection (pathogen) that is non terminal and that does not confer immunity. Thus a recovered individual can be infected again. The SIS model is implemented as a system of nodes with two possible states or compartments, susceptible state (S), and infected (I). Susceptible individuals become infected at rate λ by infected neighbours, where λ is the so-called infection rate. Infected individuals recover spontaneously at rate δ. Schematically the model can be represented as

$$S \xrightarrow{\lambda} I \xrightarrow{\delta} S. \tag{1}$$

The SIR model describes a pathogen that can be terminal or does confer immunity. Thus a recovered individual will never be infected again. The SIR model is implemented as the SIS model with an additional removed state (R), that is reached when an infected node is either recovered or dead. Schematically the model can be summarized as

$$S \xrightarrow{\lambda} I \xrightarrow{\delta} R. \tag{2}$$

The SIIR model introduced in this work simulates two SIS independent pathogens (A and B) that change their behaviour when they meet in a node. A node simultaneously infected by A and B cannot return to the susceptible state and instead passes to a removed state with a rate δ_{AB}. Figure 1 shows a sketch of the state transitions in the SIIR model.

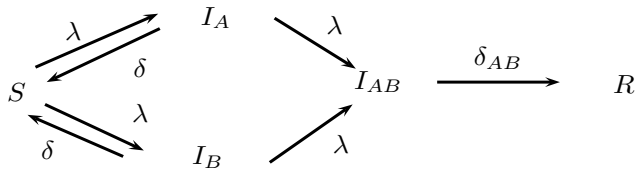

Figure 1: Sketch SIIR model.

In many cases of interest, epidemic spreading processes take place on social contact networks representing the most frequent interactions among individuals. Depending on the type of disease, these networks can be modelled as random graphs (RG) or scale-free (SF) networks. The former is a good representation of diseases like influenza whereas the latter is appropriate to model sexually transmitted diseases. RG networks are generated by the modified Erdös-Rényi algorithm [Erdös & Rényi,1959,[1]] in which each pair of nodes is connected with probability

$$p = \frac{\bar{k}}{N}, \tag{3}$$

where $\bar{k}$ is the average degree (the number of contacts per individual). This model generates very homogeneous networks with a degree distribution sharply peaked around the average $\bar{k}$. On the other hand, SF networks are characterized by a power-law degree distribution

$$P(k) \sim k^{-\gamma}, \tag{4}$$

where the degree exponent,γ, is usually found to lay between 2 and 3[2]. In this work SF networks are generated with the configuration model, as explained in appendix.

The Algorithm used to simulate the SIIR model is the Markovian Gillispie algorithm. The Gillispie algorithm [3] allows us to simulate simultaneous stochastic markovian processes, such as infection and recovery rates in SIS and SIR models.

II. EPIDEMIC MODEL AND IMPLEMENTATION OF MARKOVIAN GILLESPIE ALGORITHM

In the next subsections first we introduce the SIIR model in the mean-field approximation. Afterwords, we explain the implementation of the Markovian Gillespie algorithm.

A. Mean-field epidemic equations.

Let us consider uncorrelated homogeneous networks (RG). In the mean-field approach, the density of infected

nodes ρ evolves over time as

$$\frac{d\rho}{dt} = -\delta\rho + \lambda\bar{k}\rho(1-\rho), \tag{5}$$

where $\delta\rho$ is the rate of recovered nodes over time and $\lambda\rho(1-\rho)$ is the rate of infected nodes over time. This model predicts a threshold

$$\lambda_c = \frac{\delta}{\bar{k}} \tag{6}$$

above which the infection may survive, generating an endemic steady state for $\lambda > \lambda_c$ [5]. For $\lambda < \lambda_c$ the infection cannot survive and never become endemic.

For SF networks the same threshold can be found, [5][8]

$$\lambda_c = \frac{\bar{k}}{\bar{k^2}}. \tag{7}$$

Notice that, in the scale free regime ($2 \leq \gamma \leq 3$) this threshold is $\lambda_c = 0$ in the thermodynamic limit, meaning that any pathogen can become endemic regardless of its infectiousness.

In the SIR model the mean-field equations for uncorrelated homogeneous networks reads:

$$\frac{dS}{dt} = -\lambda\bar{k}\rho S, \tag{8}$$

$$\frac{d\rho}{dt} = -\delta\rho + \lambda\bar{k}\rho S, \tag{9}$$

$$\frac{dR}{dt} = \delta\rho. \tag{10}$$

In this model, we need to take into account that the infection always dies. So the order parameter of the infection is given by the total number of infected nodes during the outbreak. In this case, there is a threshold λ_c separating a healthy phase where the outbreak size is microscopic and an infective phase where outbreaks can reach a macroscopic fraction of the population[5]. For homogeneous networks this threshold is given by

$$\lambda_c = \frac{1}{\bar{k}}, \tag{11}$$

whereas in SF networks it is given by,[5][8],

$$\lambda_c = \frac{\bar{k}}{\bar{k^2} - \bar{k}}. \tag{12}$$

In the SIIR model infected nodes recover at rate δ_A or δ_B if they were infected with a single pathogen. Susceptible nodes become infected at rate λ_A or λ_B by contact with neighbours infected by the other pathogens. Individuals infected simultaneously by the two pathogens are removed at rate δ_{AB}, without the possibility to become susceptible again.

To write the equations we differentiate the infection rate and recuperation rate from both pathogens. In the mean-field approach, the equations for the density of infected population and removed density are:

$$\begin{aligned}\frac{d\rho_A}{dt} =& -\delta_A\rho_A \\ &+ \lambda_A\bar{k}(\rho_A + \rho_{AB})(1-\rho_A-\rho_B-\rho_{AB}-\rho_R) \\ &- \lambda_B\bar{k}\rho_A\rho_B,\end{aligned} \tag{13}$$

$$\begin{aligned}\frac{d\rho_B}{dt} =& -\delta_B\rho_B \\ &+ \lambda_B\bar{k}(\rho_B + \rho_{AB})(1-\rho_A-\rho_B-\rho_{AB}-\rho_R) \\ &- \lambda_A\bar{k}\rho_A\rho_B,\end{aligned} \tag{14}$$

$$\frac{d\rho_{AB}}{dt} = -\delta_{AB}\rho_{AB} + (\lambda_A + \lambda_B)\bar{k}\rho_A\rho_B, \tag{15}$$

$$\frac{d\rho_R}{dt} = \delta_{AB}\rho_{AB} \tag{16}$$

where $(1-\rho_A-\rho_B-\rho_{AB}-\rho_R)$ is the density of susceptible population.

Equations (13) and (14) are symmetric about the recuperation and infection. They take into account the nodes that become infected by the two pathogens through own rates, and subtract the nodes that can be infected with the rate of the other pathogen. Equation (16) remove the nodes as on SIR model.

The prevalence analysis is done through the density of removed nodes since are the ones that consider all process in the model.

B. Implementation of Gillespie Algorithm

To simulate the infection processes, we use the Gillespie Algorithm [3]. The Markovian Gillespie Algorithm follows the next steps:

1. Initialization: Randomly we infect a small number of nodes with each pathogen. In our case we infected 100 nodes for pathogen A and 100 for B in a 10000 nodes network, i.e. initially we have a 0.02% of our network infected with A or B. Since the infection is random it also can contain some nodes infected with AB.

2. Time step: Since the process is markovian, the events can be sampled as a Poisson with interevent times τ distribute as [4],

$$\phi(\tau) = N\bar{\lambda}e^{-N\bar{\lambda}\tau},$$

where $\bar{\lambda}$ is the rate of occurrence of all possible events. Thus

$$\bar{\lambda} = E_A^A\lambda_A + E_A^B\lambda_B + N_I^A\delta_A + N_I^B\delta_B + N_I^{AB}\delta_{AB},$$

where N_I^A and N_I^B are the infected nodes of A and B, respectively. E_A^A and E_A^B are actives edges of A and B, respectively. And N_I^{AB} are the infected nodes only by AB.

3. Event step: The event it's selected from it's probability of occurrence. The probability of one event is:

$$\Pi(i) = \frac{\lambda_i}{N\bar{\lambda}},$$

where λ_i is one of the events. Each event updates the state of the lattice changing E_A^A, E_A^B, N_I^A, N_I^B, N_I^{AB}.

4. Return to step 2.

For infection of A or B it is necessary to take into account that if we can have a node infected previously by the other pathogen the node infected again will be listed as AB waiting for the remove event.

III. RESULTS OF SIIR MODEL THROUGH MARKOVIAN GILLESPIE ALGORITHM

In this section we explain the results of the SIIR model implemented through Markovian Gillespie Algorithm on a Erdös-Rényi Network (RG) and on a scale-free network (SF).

First, we analyse where the endemic threshold is. Knowing this information we analyse the temporal evolution in the endemic and healthy phase.

A. Prevalence of the SIIR model

SIS and SIR models have two macroscopic states: the epidemic is either endemic or healthy. The transition between states is given by λ_c. The prevalence of the SIIR model is done through comparison of the infection rate (λ) and the density of removed nodes with different removing rates (δ_{AB}) for the RG and SF network.

Figure 2 shows that when we increase the remove state (δ_{AB}) the threshold λ increases. This happens because the infected nodes AB are removed quickly. We need a higher λ for the epidemic to become endemic. Increasing δ_{AB} does not effect much the density of removed nodes, this is because RG networks have high connectivity of the nodes. Thus nearly all nodes become removed.

As we can see on figure 3 the threshold $\lambda_c \approx 0$, as expected from theory [5][8]. But figure 3 also shows that when δ_{AB} increases the density of removed nodes decreases.

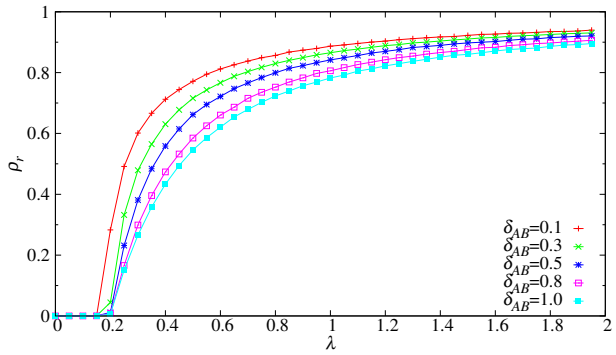

Figure 2: Mean prevalence in RG Network with 10000 nodes.

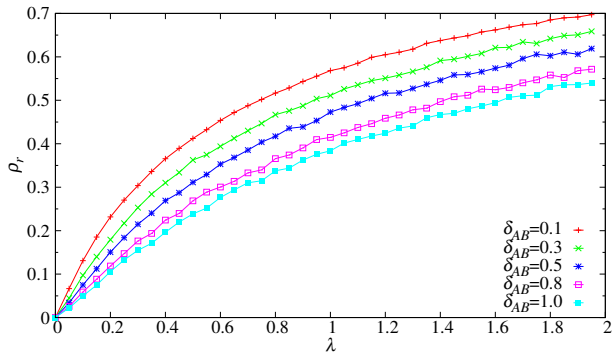

Figure 3: Mean prevalence in a SF Networks with 10000 nodes and $\gamma = 2.11$.

B. Temporal evolution of the SIIR model

We use the values of λ_c obtained through the graphs, in the last subsection, for explain the SIIR model behaviour through time.

On the figures 4-5 we can see the densities of infected nodes A and B are symmetric, as it is shown in the equations (13) and (14). And the integrated density of infected nodes from the two pathogens (AB) is proportional to the removed nodes.

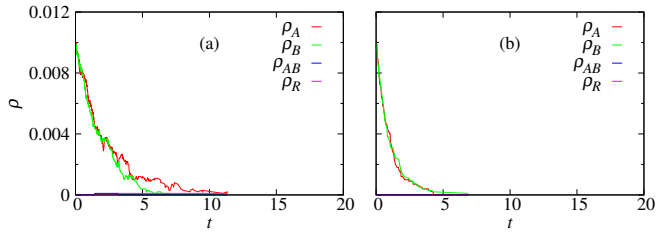

Figure 4: Temporal evolution for the networks RG and SF for $\lambda < \lambda_c$. Figure 4(a): RG with $\lambda = 0.1$, $\delta = 1$ and $\delta_{AB} = 0.4$. Figure 4(b): SF with $\lambda = 0.001$, $\delta = 1$ and $\delta_{AB} = 0.4$

As we can see in figures 4(a) and 4(b), for $\lambda < \lambda_c$ the behaviour is similar to the SIS model. This is because we are in the healthy phase and the recuperation rate (δ) is more important than λ. The nodes have no time to

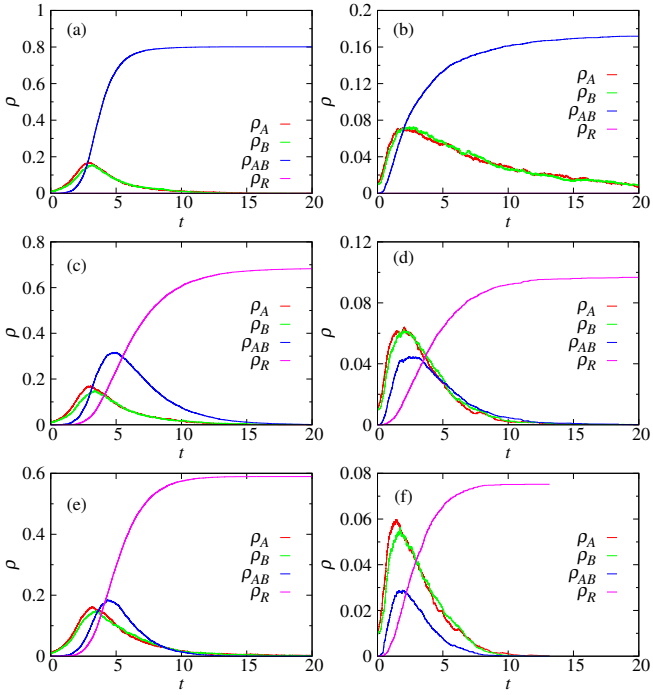

Figure 5: Temporal evolution for the networks RG and SF for $\lambda > \lambda_c$. Figure 5(a): RG with $\lambda = 0.5$, $\delta = 1$ and $\delta_{AB} = 0$. Figure 5(b): SF with $\lambda = 0.1$, $\delta = 1$ and $\delta_{AB} = 0$. Figure 5(c): RG with $\lambda = 0.5$, $\delta = 1$ and $\delta_{AB} = 0.4$. Figure 5(d): SF with $\lambda = 0.1$, $\delta = 1$ and $\delta_{AB} = 0.4$.Figure 5(e): RG with $\lambda = 0.5$, $\delta = 1$ and $\delta_{AB} = 0.8$.Figure 5(f): SF with $\lambda = 0.5$, $\delta = 1$ and $\delta_{AB} = 0.8$.

get infected by both infections before the pathogens are eradicate.

For $\lambda > \lambda_c$ the curves of the number of the infected by the two pathogens and the removed, on figures 5(c), 5(d), 5(e) and 5(f), are similar to the infected and removed density curves in the SIR model. The infected densities of one of the pathogens behave like the susceptible density on the SIR model. The reason is because we are on endemic phase and λ is high enough to become viral. On this phase a node can easily be infected by two pathogens and removed. In figures 5(a) and 5(b) we can see that when $t \to \infty$ a large fraction of nodes are infected by the two pathogens, and stuck on this state because δ_{AB} is zero. That means the state AB is an absorbing state. When we increase δ_{AB} all nodes once in the absorbing state are removed. Thus, for $t \to \infty$, all population may be is removed. We need to take into account that how much the higher δ_{AB} is the more density of removes decreases (see figures 5(c), 5(d), 5(e) and 5(f)). This is because the infected nodes from both pathogens have less time to infect other nodes and they pass directly to the remove state.

IV. CONCLUSIONS

- In a same network an in healthy phase when there is comorbidity the SIIR model is found to behave like the SIS model in endemic phase. But in endemic phase the SIIR model with comorbidity of two pathogens the behaviour is like the SIR model.

- In random graph networks when the remove rate increases the infection needs a higher λ to become endemic. Thus the interaction of the two pathogens reduce the viral spreading. However, the density of population removed is superior to the SF network.

- In scale-free networks the most connected nodes tend to become infected from both pathogens easily and thus removed. Once they are removed the epidemic loses it strength and stops. The density of removed nodes is lower than in a random graph network. The healthy phase is nearly zero, thus pathogens tend to become viral easily.

A better rigorous study of the system is needed for a better understanding in all its complexity. Since we assumed that once the nodes are infect by the two pathogens they are systematically removed. In this case the state AB is acting like an absorbing state. It could be interesting to study how results change if on AB state the node can be recovered to susceptible state for one pathogen.

Appendix A: Network generation Algorithm

In this section we explain how are generated on this work and some of their properties that are useful to understand the SIS and SIR mechanics. In both cases the networks generated are unweighed and undirected.

For the random graph we use modified Erdös-Rényi algorithm with equation (3) for determining which node of N we want to connect. Next through a we randomly choose the other node to connect. The process is repeat for al N-2 nodes.

Meanwhile for the scale-free network we use the configuration model with a power-law degree distribution (4). We assume a number of stubs according to the sampled degree. The total stubs number needs to be even in order to have all of them connected. Then randomly we will connect two stubs of a node with another stub from another node. This process is repeated until we run out of stubs. It may happen that one node can connect with itself (loop).

Both sampling methods, ER and Configuration, two models can create loops or repeated edges. So for to assure that the network is truly undirected, we implemented a program that will erase all loops and repeated edges.

Appendix B: Network properties

Once the network is generated we can measure its properties. The most important is the average number of edges per node, the so call average degree:

$$\bar{k} = \frac{1}{N}\sum_{i=1}^{N} k_i,$$

where N is the number of nodes[2].

Another important parameter is the average degree of the nearest neighbours to a node with degree k:

$$\bar{k_{nn}}(k) = \frac{1}{N_k}\sum_{i\in k} \bar{k_{nn}}(k_i), \text{ where } \bar{k_{nn}}(k_i) = \frac{1}{k_i}\sum_{j} a_{ij}k_j,$$

where a_{ij} is the adjacency matrix which will be 1 if there is an edge connecting i-j or 0 if there's no edge[2].

And the last property we want to know is the clustering coefficient, is the probability of two connected nodes of share another neighbour[2], i.e, number of triangles.

$$\bar{c}(k) = \frac{1}{N_k}\sum_{i\in k} c(k_i), \text{ where } c(k_i) = \frac{2T_i}{k_i(k_i-1)}.$$

The clustering coefficient is a good indicator of how the infection can spread on a network, since a clustered networks tend to become infected easily than a network with a lower clustering coefficient.

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