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Invited review: Epidemics on social networks

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Since its first formulations almost a century ago, mathematical models for disease spreading contributed to understand, evaluate and control the epidemic processes. They promoted a dramatic change in how epidemiologists thought of the propagation of infectious diseases. In the last decade, when the traditional epidemiological models seemed to be exhausted, new types of models were developed. These new models incorporated concepts from graph theory to describe and model the underlying social structure. Many of these works merely produced a more detailed extension of the previous results, but some others triggered a completely new paradigm in the mathematical study of epidemic processes. In this review, we will introduce the basic concepts of epidemiology, epidemic modeling and networks, to finally provide a brief description of the most relevant results in the field.

I. Introduction

With the development of more precise and powerful tools, the mathematical modeling of infectious diseases has become a crucial tool for making decisions associated to policies on public health. The scenario was completely different at the beginning of the last century, when the first mathematical models started to be formulated. The rather myopic comprehension of the epidemiological processes was evidenced during the most dramatic epidemiologic events of the last century, the pandemic 1918 flu. The lack of a mathematical understanding of the evolution of epidemics gave place to an inaccurate analysis of the epidemiological situation and subsequent failed assertion of the success of the immunization strategy. During the influenza pandemic of 1892, a viral disease, Richard Pfeiffer isolated bacteria from the lungs and sputum of patients. He installed, among the medical community, the idea that these bacteria were the cause of influenza. At that moment, the bacteria was called Pfeiffer's bacillus or Bacillus influenzae, while its present name keeps a reminiscence of Pfeiffer's wrong hypothesis: Haemophilus influenzae. Though there were some dissenters, the hypothesis of linking influenza with this pathogen was widely accepted from then on. Among the supporters of Pfeiffer hypothesis was William Park, at the New York City Health Department, who in view of the fast progression of the flu in USA, developed a vaccine and antiserum against Haemophilus influenzae on October 1918. Shortly afterwards the Philadelphia municipal laboratory released thousands of doses of the vaccine that was constituted by a mix of killed streptococcal, pneumococcal, and H. influenzae bacteria. Several other attempts to develop similar vaccines followed this initiative. However, none of these vaccines prevented viral influenza infection. The present consensus is that they were even not protective against the secondary bacterial infections associated to influenza because the

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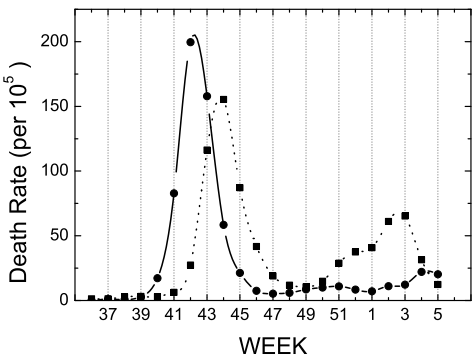

Figure 1: Weekly "Spanish influenza" death rates in Baltimore (circles) and San Francisco (squares) from 1918 to 1919. Data taken from Ref. [1].

vaccine developers at that time could not identify, isolate, and produce all the disease-causing strains of bacteria. Nevertheless, a wrong evaluation of the evolution of the disease and a lack of epidemiological knowledge led to the conclusion that the vaccine was effective. If we look at Fig. 1 corresponding to the weekly influenza death rates in a couple of U.S. cities taken from Ref. [1], we observe a remarkable decay after vaccination, in week 43. This decay was inaccurately attributed to the effect of vaccination as it corresponds actually to a normal and expected development of an epidemics without immunization.

The inaccurate association between H. influenzae and influenza persisted until 1933, when the viral etiology of the flu was established. But Pfeiffer's influenza bacillus, finally named Haemophilus influenzae, accounts in its denomination for this persistent mistake.

The formulation of mathematical models in epidemiology has a tradition of more than one century. One of the first successful examples of the mathematical explanation of epidemiological situations is associated with the study of Malaria. Ronald Ross was working at the Indian Medical Service during the last years of the 19th century when he discovered and described the life-cycle of the malaria parasite in mosquitoes and developed a mathematical model to analyze the dynamics of the transmission of the disease [2–4]. His model linked the density of mosquitoes and the incidence of malaria among the human population. Once he had identified the anopheles mosquitoes as the vector for malaria transmission, Ross conjectured that malaria could be eradicated if the ratio between the number of mosquitoes and the size of the human population was carried below a threshold value. He based his analysis on a simple mathematical model.

Ross' model was based on a set of deterministic coupled differential equations. He divided the human population into two groups, the susceptible, with proportion S_h and the infected, with proportion I_h. After recovery, any formerly infected individual returned to the susceptible class. This is called a SIS model. The mosquito population was also divided into two groups (with proportions S_m and I_m), with no recovery from infection. Considering equations for the fraction of the population in each state, we have $S + I = 1$ for both humans and mosquitoes and the model is reduced to a set of two coupled equations

$$\begin{aligned} \frac{dI_h}{dt} &= abfI_m(1 - I_h) - rI_h \qquad (1) \\ \frac{dI_m}{dt} &= acI_h(1 - I_m) - \mu_m I_m, \end{aligned}$$

where a is the man biting rate, b is the proportion of bites that produce infection in humans, c is the proportion of bites by which one susceptible mosquito becomes infected, f is the ratio between the number of female mosquitoes and humans, r is the average recovery rate of human and μ_m is the rate of mosquito mortality.

One of the parameters to quantify the intensity of the epidemics propagation is the basic reproductive rate R_0, that measures the average number of cases produced by an initial case throughout its infectious period. R_0 depends on several factors. Among them, we can mention the survival time of an infected individual, the necessary dose for infection, the duration of infectiousness in the host, etc. R_0 allows to determine whether or not an infectious disease can spread through a population: an infection can spread in a population only if $R_0 > 1$ and can be maintained in an endemic state when $R_0 = 1$ [5]. In the case of malaria, R_0 is defined as the number of secondary cases of malaria arising from a single case in an susceptible population. For

the model described by Eq. (1)

$$R_0 = \frac{ma^2bc}{r\mu_m}. \tag{2}$$

It is clear that the choice of the parameters affects R_0. The main result is that it is possible to reduce R_0 by increasing the mosquito mortality and reducing the biting rate. For his work on malaria, Ross was awarded the Nobel Prize in 1902.

Ross' pioneering work was later extended to include other ingredients and enhance the predictability power of the original epidemiological model [5–11].

Some years after Ross had proposed his model, a couple of seminal works established the basis of the current trends in mathematical epidemiology. Both models consider the population divided into three epidemiological groups or compartments: susceptible (S), infected (I) and recovered (R).

On the one hand, Kermack and McKendrick [12] proposed a SIR model that expanded Ross' set of differential equations. The model did not consider the existence of a vector, but a direct transmission from an infected individual to a susceptible one. A particular case of the original model, in which there is no age dependency of the transmission and recovery rate, is the classical SIR model that will be explained later.

On the other hand, Reed and Frost [13] developed a SIR discrete and stochastic epidemic model to describe the relationship between susceptible, infected and recovered immune individuals in a population. It is a chain binomial model of epidemic spread that was intended mainly for teaching purposes, but that is the starting point of many modern epidemiological studies. The model can be mapped into a recurrence equation that defines what will happen at a given moment depending on what has happened in the previous one,

$$I_{t+1} = S_t(1 - (1 - \rho)^{I_t}), \tag{3}$$

where I_t is the number of cases at time t, S_t is the number of susceptible individuals at time t and ρ is the probability of contagion.

The basic assumption of these SIR models, which is present in almost any epidemiological work, is that the infection is spread directly from infectious individuals to susceptible ones after a certain type of interaction between them. In turn, these newly infected individuals will develop the infection to become infectious. After a defined period of time, the infected individuals heal and remain permanently immune. The interaction between any two individuals of the population is considered as a stochastic process with a defined probability of occurrence that most of the deterministic model translates into a contact rate.

Given a closed population and the number of individuals in each state, the calculation of the evolution of the epidemics is straightforward. The epidemic event is over when no infective individuals remain.

While many classic deterministic epidemiological models were having success at describing the dynamics of an infectious disease in a population, it was noted that many involved processes could be better described by stochastic considerations and thus a new family of stochastic models was developed [14–19]. Sometimes, deterministic models introduce some colateral mistakes due to the continuous character of the involved quantities.An example of such a case is discussed in Ref. [20]. In Ref. [21], the authors proposed a deterministic model to describe the prevalence of rabies among foxes in England. They predicted a sharp decaying prevalence of the rabies up to negligible levels, followed by an unexpected new outbreak of infected foxes. The spontaneous outbreak after the apparent disappearing of the rabies is due to a fictitious very low endemic level of infected foxes, as explained in Ref. [20]. The former one is one among several examples of how stochastic models contributed to a better understanding and explanation of some observed phenomena but, as their predecessors, they considered a mean field scheme in the set of differential equations.

Traditional epidemiological models have successfully describe the generalities of the time evolution of epidemics, the differential effect on each age group, and some other relevant aspects of an epidemiological event. But all of them are based on a fully-mixing approximation, proposing that each individual has the same probability of getting in touch with any other individual in the population. The real underlying pattern of social contacts shows that each individual has a finite set of acquaintances that serve as channels to promote the contagion. While the fully mixed approximation allows for writing down a set of differential equations

and a further exploitation of a powerful analytic set of tools, a better description of the structure of the social network provides the models with the capacity to compute the epidemic dynamics at the population scale from the individual-level behavior of infections, with a more accurate representation of the actual contact pattern. This, in turn, reflects some emergent behavior that cannot be reproduced with a system based on a set of differential equation under the fully mixing assumption. One of the most representative examples of this behavior is the so called herd immunity, a form of immunity that occurs when the vaccination of a significant portion of the population is enough to block the advance of the infection on other non vaccinated individuals. Additionally, some network models allow also for an analytic study of the described process. It is not surprising then that during the last decade, a new tendency in epidemiological modeling emerged together with the inclusion of complex networks as the underlying social topology in any epidemic event. This new approach proves to contribute with a further understanding of the dynamics of an epidemics and unveils the crucial effect of the social architecture in the propagation of any infectious disease.

In the following section, we will introduce some generalities about traditional epidemiological models. In section III, we will present the most commonly used complex networks when formulating an epidemiological model. In section IV, we will describe the most relevant results obtained by modeling epidemiological processes using complex networks to describe the social topology. Next, we will introduce the concept of herd protection or immunity and a discussion of some of the works that treat this phenomenon.

II. Basic Epidemiological Models

Two main groups can be singled out among the deterministic models for the spread of infectious diseases which are transmitted through person-to-person contact: the SIR and the SIS. The names of these models are related to the different groups considered as components of the population or epidemiological compartments: S corresponds to susceptible, I to infected and R to removed. The S group represents the portion of the population that has not been affected by the disease but may be infected in case of contact with a sick person. The I group corresponds to those individuals already infected and who are also responsible for the transmission of the disease to the susceptible group. The removed group R includes those individuals recovered from the disease who have temporary or permanent immunity or, eventually, those who have died from the illness and not from other causes. These models may or may not include the vital dynamics, associated with birth and death processes. Its inclusion depends on the length of time over which the spread of the disease is studied.

i. The SIR Model

As mentioned before, in 1927, Kermack and McKendrick [12] developed a mathematical model in which they considered a constant population divided into three epidemiological groups : susceptible, infected and recovered. The equations of a SIR model are

$$\begin{aligned} \frac{dS}{dt} &= -\beta SI \\ \frac{dI}{dt} &= \beta SI - \gamma I \\ \frac{dR}{dt} &= \gamma I, \end{aligned} \tag{4}$$

where the involved quantities are the proportion of individuals in each group. As the population is constant,

$$S(t) + I(t) + R(t) = 1. \tag{5}$$

The SIR model is used when the disease under study confers permanent immunity to infected individuals after recovery or, in extreme cases, it kills them. After the contagious period, the infected individual recovers and is included in the R group. These models are suitable to describe the behavior of epidemics produced by virus agent diseases (measles, chickenpox, mumps, HIV, poliomyelitis) [22].

The model formulated through Eq. (4) assumes that all the individuals in the population have the same probability of contracting the disease with a rate of β, the contact rate. The number of infected increases proportionally to both the number

of infected and susceptible. The rate of recovery or removal is proportional to the number of infected only. γ represents the mean recovery rate, ($1/\gamma$ is the mean infective period). It is assumed that the incubation time is negligible and that the rates of infection and recovery are much faster than the characteristic times associated to births and deaths. Usually, the initial conditions are set as

$$S(0) > 0, \;\; I(0) > 0 \text{ and } R(0) = 0. \tag{6}$$

It is straightforward to show that

$$\left.\frac{dI}{dt}\right|_{t=0} = I(0)(\beta S(0) - \gamma), \tag{7}$$

and that the sign of the derivative depends on the value of $S_c = \frac{\gamma}{\beta}$. When $S(t) > S_c$, the derivative is positive and the number of infected individuals increases. When $S(t)$ goes below this threshold, the epidemic starts to fade out.

A rather non intuitive result can be obtained from Eq. 4. We can write

$$\begin{aligned} \frac{dS}{dR} &= -\frac{S}{\rho} \\ &\Rightarrow \quad S = S_0 \exp[-R/\rho] \geq S_0 \exp[-N/\rho] > 0 \\ &\Rightarrow \quad 0 < S(\infty) \leq N. \end{aligned} \tag{8}$$

The epidemics stops when $I(t) = 0$, so we can set $I(\infty) = 0$, so $R(\infty) = N - S(\infty)$. From (8),

$$\begin{aligned} S(\infty) &= S_0 \exp\left[-\frac{R(\infty)}{\rho}\right] \\ &= S_0 \exp\left[-\frac{N - S(\infty)}{\rho}\right]. \end{aligned} \tag{9}$$

The last equation is a transcendent expression with a positive root $S(\infty)$.

Taking (9), we can calculate the total number of susceptible individuals throughout the whole epidemic process

$$I_{\text{total}} = I_0 + S_0 - S(\infty). \tag{10}$$

As $I(t) \to 0$ and $S(t) \to S(\infty) > 0$, we conclude that when the epidemics end, there is a portion of the population that has not been affected

The previous model can be extended to include vital dynamics [23], delays equations [24], age structured population, migration [25], and diffusion. In any case, all these generalizations only introduce some slight changes on the steady states of the system, or in the case of spatially extended models, travelling waves [26].

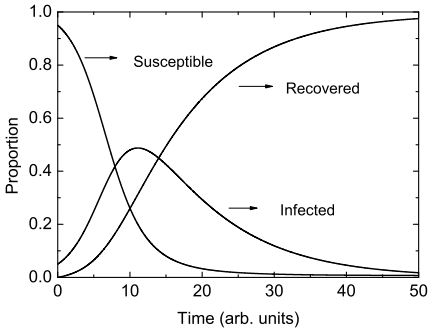

Figure 2: Temporal behavior of the proportion of individuals in each of the three compartments of the SIR model.

Figure 2 displays the typical behavior of the density of individuals in each of the epidemiological compartments described by Eq. (4). Compare this with the pattern shown in Fig. 1.

ii. The SIS Model

The SIS model assumes that the disease does not confer immunity to infected individuals after recovery. Thus, after the infective period, the infected individual recovers and is again included in the S group. Therefore, the model presents only two epidemiological compartments, S and I. This model is suitable to describe the behavior of epidemics produced by bacterial agent diseases (meningitis, plague, venereal diseases) and by protozoan agent diseases (malaria) [22]. We can write the equations for a general SIS model assuming again that the population is constant,

$$\begin{aligned} \frac{dS}{dt} &= -\beta SI + \gamma I \\ \frac{dI}{dt} &= \beta SI - \gamma I. \end{aligned} \tag{11}$$

As the relation $S + I = 1$ holds, Eq. (11) can be reduced to a single equation,

$$\frac{dI}{dt} = (\beta - \gamma)I - \beta I^2. \tag{12}$$

The solution of this equation is

$$I(t) = (1 - \frac{\gamma}{\beta}) \frac{C \exp[(\gamma - \beta)t]}{1 + C \exp[(\gamma - \beta)t]}, \qquad (13)$$

where C is defined by the initial conditions as

$$C = \frac{\beta i_0}{\beta(1 - i_0) - \gamma}. \qquad (14)$$

If I_0 is small and $\beta > \gamma$, the solution is a logistic growth that saturates before the whole population is infected, the stationary value is $I_s = \frac{\beta - \gamma}{\beta}$. It can be shown that $R_0 = \beta/\gamma$. This sets the condition for the epidemic to persist.

iii. Other models

The literature on epidemiological models includes several generalizations about the previous ones to adapt the description to the particularities of a specific infectious disease [27]. One possibility is to increase the number of compartments to describe different stages of the state of an individual during the epidemic spread. Among these models, we can mention the SIRS, a simple extension of the SIR that does not confer a permanent immunity to recovered individuals and after some time they rejoin the susceptible group,

$$\begin{aligned} \frac{dS}{dt} &= -\beta SI + +\lambda R \\ \frac{dI}{dt} &= \beta SI - \gamma I \\ \frac{dR}{dt} &= \gamma I - \lambda R. \end{aligned} \qquad (15)$$

Other models include more epidemiological groups or compartments, such as the SEIS and SEIR model, that take into consideration the exposed or latent period of the disease, by defining an additional compartment E.

There are several diseases in which there is a vertical transient immunity transmission from a mother to her newborn. Then, each individual is born with a passive immunity acquired from the mother. To indicate this, an additional group P is added.

The range of possibilities is rather extended, and this is reflected in the title of Ref. [27]: "A thousand and one epidemiological models". There are a lot of possibilities to define the compartment structure. Usually, this structure is represented as a transfer chart indicating the flow between the compartments and the external contributions. Figure 3 shows an example of a diagram for a SEIRS model, taken from Ref. [27].

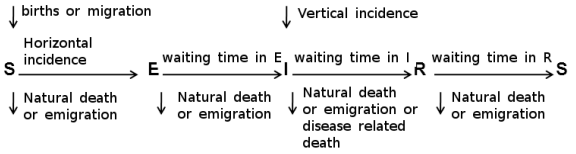

Figure 3: Transfer diagram for a SEIRS models. Taken from Ref. [27].

Horizontal incidence refers to a contagion due to a contact between a susceptible and infectious individual, vertical incidence account for the possibility for the offspring of infected parents to be born infected, such as with AIDS, hepatitis B, Chlamydia, etc.

Many of the previous models have been expanded, including stochastic terms. One of the most relevant differences between the deterministic and stochastic models is their asymptotic behavior. A stochastic model can show a solution converging to the disease-free state when the deterministic counterpart predicts an endemic equilibrium. The results obtained from the stochastic models are generally expressed in terms of the probability of an outbreak and of its size and duration distribution [14–19].

III. Complex Networks

A graph or network is a mathematical representation of a set of objects that may be connected between them through links. The interconnected objects are represented by the nodes (or vertices) of the graph while the connecting links are associated to the edges of the graph. Networks can be characterized by several topological properties, some of which will be introduced later. Social links are preponderantly non directional (symmetric), though there are some cases of social directed networks. The set of nodes attached to a given node through these links is called its neighborhood. The size of the neighborhood is the degree of the node.

While the study of graph theory dates back to the

pioneering works of Erdös and Renyi in the 1950s [28], their gradual colonization of the modern epidemiological models has only started a decade ago. The attention of modelers was drawn to graph theory when some authors started to point out that the social structure could be mimicked by networks constructed under very simple premises [30, 34]. Since then, a huge collection of computer-generated networks have been studied in the context of disease transmission. The underlying rationale for the use of networks is that they can represent how individuals are distributed in social and geographical space and how the contacts between them are promoted, reinforced or inhibited, according to the rules of social dynamics. When the population is fully mixed, each individual has the same probability of coming into contact with any other individual. This assumption makes it possible to calculate the effective contact rates β as the product of the transmission rate of the disease, the effective number of contacts per unit time and the proportion of these contacts that propagate the infection. The formulation of a mean field model is then straightforward. However, in real systems, the acquaintances of each individual are reduced to a portion of the whole population. Each person has a set of contacts that shapes the local topology of the neighborhood. The whole social architecture, the network of contacts, can be represented with a graph.

In the limiting case when the mean degree of the nodes in a network is close to the total number of nodes, the difference between a structured population and a fully mixed one fades out. The differences are noticeable when the network is diluted, i.e., the mean degree of the node is small compared with the size of the network. This will be a necessary condition for all the networks used to model disease propagation. In the following paragraphs, we will introduce the most common families of networks used for epidemiological modeling.

Lattices. When incorporating a network to a model, the simplest case is considering a grid or a lattice. In a squared d dimensional lattice, each node is connected to $2d$ neighbors. Individuals are regularly located and connected with adjacent neighbors; therefore, contacts are localized in space. Figure 4 shows, among others, an example of a two dimensional square lattice

Small-world networks. The concept of *Small World* was introduced by Milgram in 1967 in order

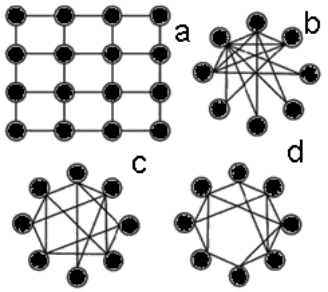

Figure 4: Scheme of four kinds of networks: (a) Lattice, (b)scale free, (c) Exponential, (d) Small World.

to describe the topological properties of social communities and relationships [29]. Some years ago, Watts and Strogatz introduced a model for constructing networks displaying topological features that mimic the social architecture revealed by Milgram. In this model of Small World (SW) networks a single parameter p, running from 0 to 1, characterizes the degree of disorder of the network, ranging from a regular lattice to a completely random graph [30]. The construction of these networks starts from a regular, one-dimensional, periodic lattice of N elements and coordination number $2K$. Each of the sites is visited, rewiring K of its links with probability p. Values of p within the interval [0,1] produce a continuous spectrum of small world networks. Note that p is the fraction of modified regular links. A schematic representation of this family of networks is shown in Fig. 5.

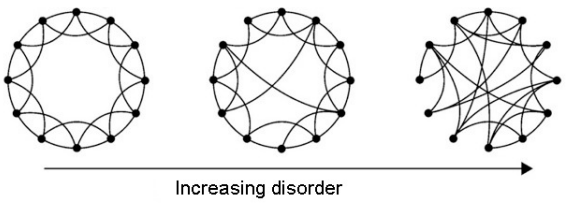

Figure 5: Representation of several Small World Networks constructed according the algorithm presented in Ref. [30]. As the disorder degree increases, there number of shortcuts grow replacing some of the original (ordered network) links.

To characterize the topological properties of the

SW networks, two magnitudes are calculated. The first one, $L(p)$, measures the mean topological distance between any pair of elements in the network, that is, the shortest path between two vertices, averaged over all pairs of vertices. Thus, an ordered lattice has $L(0) \sim N/K$, while, for a random network, $L(1) \sim ln(N)/ln(K)$. The second one, $C(p)$, measures the mean clustering of an element's neighborhood. $C(p)$ is defined in the following way: Let us consider the element i, having k_i neighbors connected to it. We denote by $c_i(p)$ the number of neighbors of element i that are neighbors among themselves, normalized to the value that this would have if all of them were connected to one another; namely, $k_i(k_i-1)/2$. Now, $C(p)$ is the average, over the system, of the local clusterization $c_i(p)$. Ordered lattices are highly clustered, with $C(0) \sim 3/4$, and random lattices are characterized by $C(1) \sim K/N$. Between these extremes, small worlds are characterized by a short length between elements, like random networks, and high clusterization, like ordered ones.

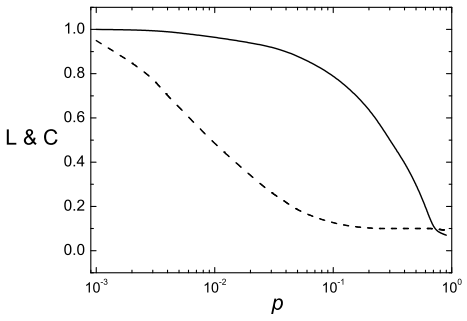

Figure 6: In this figure, we show the mean values of the clustering coefficient C and the path length L as a function of the disorder parameter p. Note the fast decay of L and the presence of a region where the value adopted by L is similar to the one corresponding to total disorder, while the value adopted by C is close to the one corresponding to the ordered case.

Other procedures for developing similar social networks have been proposed in Ref. [31] where instead of rewiring existing links to create shortcuts, the procedure add links connecting two randomly chosen nodes with probability p. In Fig. 7, we show an example, analogous to the one shown in Fig. 5.

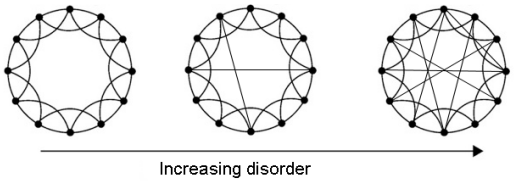

Figure 7: Representation of several Small World Networks constructed according the algorithm presented in Ref. [31]. As the disorder degree increases, three number of shortcuts as well as the number of total links grow.

Random networks. There are different families of networks with random genesis but displaying a wide spectra of complex topologies. In random networks, the spatial position of individuals is irrelevant and the links are randomly distributed. The iconic Erdös-Rényi (ER) random graphs are built from a set of nodes that are randomly connected with probability p, independently of any other existing connection. The degree distribution, i.e., the number of links associated to each node, is binomial and when the number of nodes is large, it can be approximated by a Poisson distribution [32]. In Ref. [33], the authors propose a formalism based on the generating function that permits to construct random networks with arbitrary degree distribution. The mechanism of construction also allows for further analytic studies on these networks. In particular, networks can be chosen to have a power law degree distribution. This case will be presented in the next paragraphs.

Scale-free network. As mentioned before, one of the most revealing measures of a network is its degree of distribution, i.e., the distribution of the number of connections of the nodes. In most real networks, it is far from being homogeneous, with highly connected individuals on one extreme and almost isolated nodes on the other. Scale-free networks provide a means of achieving such extreme levels of heterogeneity.

Scale-free networks are constructed by adding new individuals to a core, with a connection mechanism that imitates the underlying process that rules

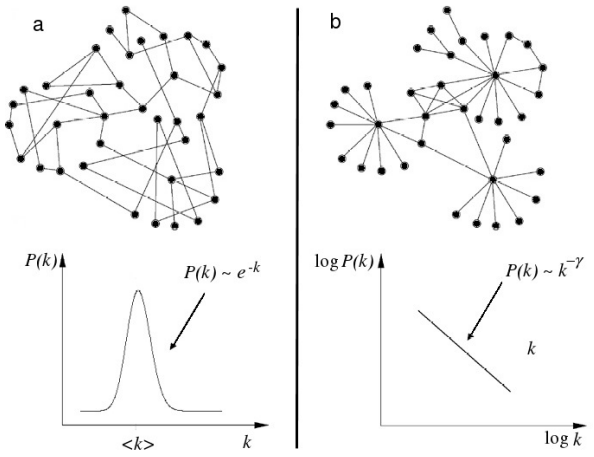

Figure 8: This figure shows examples of (a) ER and (b) BA networks. The figure also displays the connectivity distribution $P(k)$, that follows a binomial distribution for the ER networks and a power law for BA networks.

the choice of social contacts. The Barabási - Albert (BA) model algorithm, one of the triggers of the present huge interest on scale-free networks, uses a preferential attachment mechanism [34]. The algorithm starts from a small nucleus of connected nodes. At each step, a new node is added to the network and connected to m existing nodes. The probability of choosing a node p_i is proportional to the number of links that the existing node already has

$$p_i = \frac{k_i}{\sum_j k_j},$$

where k_i is the degree of node i. That means that the new nodes have a preference to attach themselves to the most "popular" nodes. One salient feature of these networks is that their degree distribution is scale-free, following a power law of the form

$$P(k) \sim k^{-3}.$$

A sketch of the typical topology of the last two networks is shown in Fig. 8. While the degree distribution of the ER network has a clear peak and is close to homogeneous, the topology of the BA network is dominated by the presence of hub, highly connected nodes. The figure also displays the typical degree distribution $P(k)$ for each case.

Over the last years, many other attachment mechanisms have been proposed to obtain scale-free networks with other adjusted properties such as the clustering coefficient, higher moments of the degree distribution [35–38].

Coevolutive or adaptive topology. When one of the former examples of networks is chosen as a model for the social woven, there is an implicit assumption: the underlying social topology is frozen. However, this situation does not reflect the observed fact that in real populations, social and migratory phenomena, sanitary isolation or other processes can lead to a dynamic configuration of contacts, with some links being eliminated, other being created. If the time span of the epidemics is long enough, the social network will change and these changes will not be reflected if the topology remains fixed. This is particularly important in small groups. The social dynamics, including the epidemic process, can shape the topology of the network, creating a feedback mechanism that can favor or attempt against the propagation of an infectious disease. For this reason, some models consider a coevolving network, with dynamic links that change the aspect of the networks while the epidemics occur.

IV. Epidemiological Models on Networks

In this section, we will discuss several models based on the use of complex networks to mimic the social architecture. The discussion will be organized according to the topology of these underlying networks.

Lattices. Lattices were the first attempt to represent the underlying topology of the social contacts and thus to analyze the possible effect of interactions at the individual level. These models took distance from the paradigmatic fully mixed assumption and focused on looking for those phenomena that a mean field model could not explain. Still, the lattices cannot fully capture the role of inhomogeneities. As the individuals are located on a regular grid, mostly two dimensional, the neighborhood of each node is reduced to the adjacent nodes, inducing only short range or localized interactions. A typical model considers that the nodes can be in any of the epidemiological states or compartments.

The dynamic of the epidemics evolves through a contact process [39] and the evolutive rules do not differ too much from traditional cellular automata models [40]. Disease transmission is modeled as a stochastic process. Each infected node has a probability p_i of infecting a neighboring susceptible node. Once infected, the individuals may recover from infection with a probability p_r; i.e., the infective stage lasts typically $1/p_r$. From the infective phase, the individuals can move back to the susceptible compartment or the recovered phase, depending on whether the models are SIS or SIR. Usually, a localized infectious focus is introduced among the population. The transient shows a local and slow development of the disease that at the initial stage involves the growing of a cluster, with the infection propagating at its boundary, like a traveling wave. After the initial transient, SIS, SIR and SIRS models behave in different ways. The initially local dynamics that can or cannot propagate to the whole system is what introduces a completely new behavior in this spatially extended model. In Ref. [41], the author argued the infective clusters behave as the clusters in the directed percolation model. Figure 9 shows an example of the behavior of the asymptotic value of infected individuals under SIS dynamics in a two dimensional square lattice. The figure reflects the results found in Ref. [42]. The parameter f is associated to the infectivity of infectious individuals, closely related to the contact rate. We observe the inset displaying the scaling of the data with a power-like curve $A|f - f_c|^\alpha$, with $\alpha \approx 0.5$ [42].

As mentioned before, Kermack and Mckendrick [12] proved the existence of a propagation threshold for the disease invading a susceptible population. The lattice based SIR models introduce a different threshold. The simulations show that epidemics can just remain localized around the initial focus or turn into a pandemic, affecting the entire population. The most dramatic examples of real pandemic are the Black Plague between the 1300 and 1500 and the Spanish Flu, in 1917-1918. Both left a wake of death and terror while crossing the European continent. The predicted new threshold established a limit below in which the pandemic behaviour is not achieved.

Some works about epidemic propagation on lattices are analogous to forest fire models [43], with the characteristic feature that the frequency distributions of the epidemic sizes and duration obey a power-law. In Ref. [44, 45], the authors exploit these analogies to explain the observed behavior of measles, whooping cough and mumps in the Faroe Islands. The observed data display a power-like behavior.

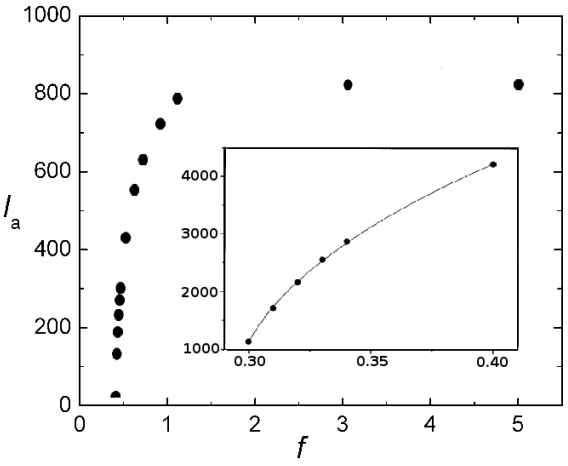

Figure 9: SIS model. Asymptotic value of infected individuals as a function of the infectivity of infectious individuals. The inset displays the scaling of the data with a power-like curve $A|f - f_c|^\alpha$, with $\alpha \approx 0.5$. Adapted from Ref. [42].

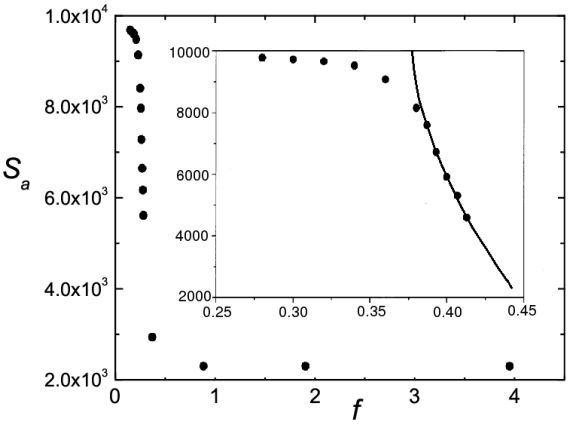

Figure 10: SIR model. Asymptotic value of susceptible individuals as a function of the infectivity of infectious individuals. The inset displays the scaling of the data with a power-like curve $A|f - f_c|^\alpha$, with $\alpha \approx 0.5$. Adapted from Ref. [42].

Random networks. Most of the models based on random graphs were previous to the renewed interest on complex networks. A simple but effective idea for the study of the dynamics of diseases on random networks is the contact process proposed in Ref. [46] that produces a branching phenomena while the infection propagates. In Ref. [47], the authors use a E-R network with an approximately Poisson degree distribution. A common feature to all these models is that the rate of the initial transient growth is smaller than the corresponding to similar models in fully-mixed populations. This effect can be easily understood noting that, on the one hand, the degree of a given initially infected node is typically small, thus having a limited number of susceptible contacts. On the other hand, there is a self limiting process due to the fact that the same infection propagation predates the local availability of susceptible targets.

A different analytical approach to random networks is presented in Ref. [48]. The author shows that a family of variants of the SIR model can be solved exactly on random networks built by a generating function method and appealing to the formalism of percolation models. The author analyzes the propagation of a disease in networks with arbitrary degree distributions and heterogeneous infectiveness times and transmission probabilities. The results include the particular case of scale-free networks, that will be discussed later.

Small-world networks. As mentioned above, regular networks can exhibit high clustering but long path lengths. On the other extreme, random networks have a lot of shortcuts between two distant individuals, but a negligible clustering. Both features affect the propagative behavior on any modeled disease. The spread of infectious diseases on SW networks has been analyzed in several works. The interested was triggered by the fact that even a small number of random connections added to a regular lattice, following for example the algorithm described in Ref. [30], produces unexpected macroscopic effects. By sharing topological properties from random and ordered networks, SW networks can display complex propagative patterns. On the one hand, the high level of clustering means that most infection occurs locally. On the other hand, shortcuts are vehicles for the fast spread of the epidemic to the entire population.

In Ref. [51], the authors study a SI model and show that shortcuts can dramatically increase the possibility of an epidemic event. The analysis is based on bond percolation concepts. While the result could be easily anticipated due to the long range propagative properties of shortcuts, the authors find an important analytic result. It was a study of a SIRS models that showed for the first time the evidence of a dramatic change in the behavior of an epidemic due to changes in the underlying social topology [52]. By specifically analyzing the effect of clustering on the dynamics of an epidemics, the authors show that a SIRS model on a SW network presents two distinct types of behavior. As the rewiring parameter p increases, the system transits from an endemic state, with a low level of infection to periodic oscillations in the number of infected individuals, reflecting an underlying synchronization phenomena. The transition from one regime to the other is sharp and occurs at a finite value of p. The reason behind this phenomenon is still unknown. Figure 11 shows the temporal behavior of the number of infected individuals for three values of the rewiring parameter p, as found in Ref. [52].

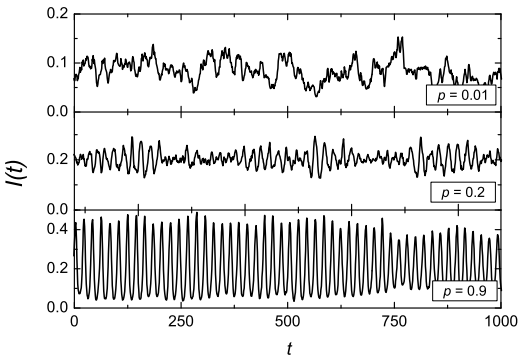

Figure 11: Asymptotic behavior of the number of infected individuals in three SW networks with different degrees of disorder p. The emergence of a synchronized pattern is evident in the bottom graph.

It would not be responsible to affirm that SW networks reflect all the real social structures. However, they capture essential aspects of such organization that play central roles in the propagation

of a diseases, namely, the clustering coefficient and the short social distance between individuals. Understanding that there are certain limitations, SW networks help to mimic different social organizations that range from rural population to big cities. There are more sophisticated models of networks with topologies that are more closely related to real social organizations at large scale. These networks are characterized by a truncated power law distribution of the degree of the nodes and by values of clustering and mean distance corresponding to the small world regime.

Scale-free networks. Scale-free networks captured the attention of epidemiologists due to the close resemblance between their extreme degree distribution and the pattern of social contacts in real populations. A power law degree distribution presents individuals with many contacts and who play the role of super-spreaders. A higher number of contacts implies a greater risk of infection and correspondingly, a higher "success" as an infectious agent. Some scale-free networks present positive assortativity. That translates into the fact that highly connected nodes are connected among them. This local structures can be used to model the existence of core groups of high-risk individuals, that help to maintain sexually transmitted diseases in a population dominated by long-term monogamous relationships [53]. Models of disease spread through scale-free networks showed that the infection is concentrated among the individuals with highest degree [48, 54]. One of the most surprising results is the one found in Ref. [54]. There, the authors show that no matter the values taken by the relevant epidemiological parameter, there is no epidemic threshold. Once installed in a scale-free network, the disease will always propagate, independently of R_0. Remember that when analyzed under the fully mixed assumption, the studied SIS model has a threshold. The authors perform analytic and numerical calculations of the propagation of the disease, to show the lack of thresholds. Later, in Ref. [55], it was pointed out that networks with divergent second moments in the degree distribution will show no epidemic threshold. The B A network fulfills this condition. In Ref. [56, 57], the authors analyze the structure of different networks of sexual encounters, to find that it has a pattern of contact closely related to a power law. They also discuss the implications of such structure on the propagation of venereal diseases

Co-evolutionary networks. Co-evolutionary or adaptive networks take into account the own dynamics of the social links. In some occasions, the characteristic times associated to changes in social connections are comparable with the time scales of an epidemic process. Some other times, the presence of n infectious core induces changes in social links. Consider for example a case when the population of susceptible individuals after learning about the existence of infectious individuals try to avoid them, or another case when the health policies promote the isolation of infectious individuals [58]. The behavior of models based on adaptive network is determined by the interplay of two different dynamics that sometimes have competitive effects. On the one hand, we have the dynamics of the disease propagation. On the other hand, the network dynamics that operates to block the advance of the infection. The later is dominated by the rewiring rate of the network, which affects the fraction of susceptible individuals connected to infective ones. The most obvious choice is to eliminate the infectious contacts of a susceptible individual by deleting or replacing them with noninfectious ones. The net effect is an effective reduction of the infection rate. While static networks typically predict either a single attracting endemic or disease-free state, the adaptive networks show a new phenomenon, a bistable situation shared by both states. The bistability appears for small rewiring rates [58–61]. In Ref. [61], the authors consider a contact switching dynamics. All links connecting a susceptible agents with an infective one is broken with a rate r. The susceptible node is then connected to a new neighbor, randomly chosen among the entire population. The authors show that reconnection can completely prevent an epidemics, eliminating the disease. The main conclusion is that the mechanism that they propose, contact switching, is a robust and effective control strategy. Figure 12 displays the results found in Ref. [61], where two completely different types of behavior can be distinguish as the rewiring parameter r changes. The crossover from one regime to the other is a second order phase transition.

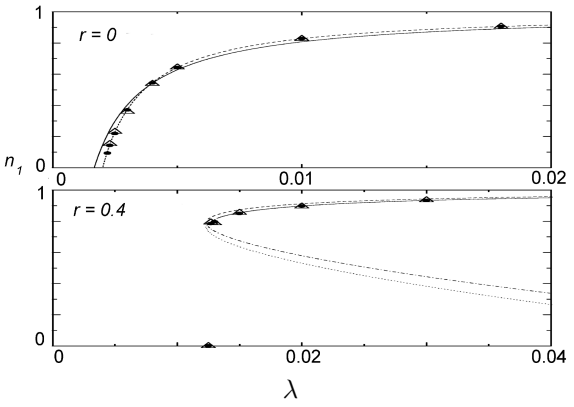

Figure 12: These two panels show the equilibrium fraction number of infected individuals, as a function of the infectivity of the disease, λ. Lines are analytic results, symbols are numerical simulations. Adapted from Ref. [61].

V. Immunization in networks

Any epidemiological model can reproduce the fact that the number of individuals in a population who are effectively immune to a given infection depends on the proportion of previously infected individuals and the proportion who have been efficiently vaccinated.

For some time, the epidemiologists knew about an emerging effect called herd protection (or herd immunity). They discovered the occurrence of a global immunizing effect verified when the vaccination of a significant portion of a population provides protection for individuals who have not or cannot developed immunity. Herd protection is particularly important for diseases transmitted from person to person. As the infection progresses through the social links, its advance can be disrupted when many individuals are immune and their links to non immune subjects are no longer valid channels of propagation. The net effect is that the greater the proportion of immune individuals is, the smaller the probability that a susceptible individual will come into contact with an infectious one. The vaccinated individuals will not contract neither transmit the disease, thus establishing a firewall between infected and susceptible individuals.

While taking profit from the herd protection is far from being an optimal public health policy, it is still taken into consideration when individuals cannot be vaccinated due, for example, to immune disorders or allergies. The herd protection effect is equivalent to reduce the R_0 of a disease. There is a threshold value for the proportion of necessary immune individuals in a population for the disease not to persist or propagate. Its value depends on the efficacy of the vaccine but also on the virulence of the disease and the contact rate. If the herd effect reduces the risk of infection among the uninfected enough, then the infection may no longer be sustainable within the population and the infection may be eliminated. In a real population, the emergence of herd immunity is closely related to the social architecture. While many fully mixed models can describe the phenomenon, the real effect is much more accurately reproduced by models based on Social Networks. One of the most expected result is to quantify how the shape of a social network can affect the level of vaccination required for herd immunity. There is a related phenomenon, not discussed here, that consists in the propagation of real immunity from a vaccinated individual to a non vaccinated one. This is called contact immunity and has been verified for several vaccines, such as the OPV [62].

The models to quantify the success of immunization of the population propose a targeted immunization of the populations.

It is well established that immunization of randomly selected individuals requires immunizing a very large fraction of the population, in order to arrest epidemics that spread upon contact between infected individuals.

In Ref. [63], the authors studied the effects of immunization on an SIR epidemiological model evolving on a SW network. In the absence of immunization, the model exhibits a transition from a regime where the disease remains localized to a regime where it spreads over a portion of the system. The effect of immunization reveals through two different phenomena. First, there is an overall decrease in the fraction of the population affected by the disease. Second, there is a shift of the transition point towards higher values of the disorder. This can be easily understood as the effective average number of susceptible neighbors per individual decreases. Targeted immunization that is applied by vaccinating those individuals with the highest de-

gree, produces a substantial improvement in disease control. It is interesting to point out that this improvement occurs even when the degree distribution over small-world networks is relatively uniform, so that the best connected sites do not monopolize a disproportionately high number of links. Figure 13 shows an example of the results found in Ref. [63], where the author compare the amount of non vaccinated individuals that are infected for different levels of vaccination, ρ, and different degrees of disorder of the SW network p, as defined in Ref. [30].

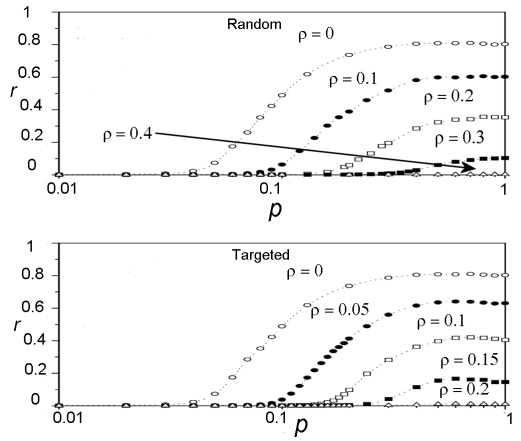

Figure 13: Fraction r of the non-vaccinated population that becomes infected during the disease propagation, as a function of the disorder parameter p, for various levels of random immunization (upper) and targeted immunization (bottom). Adapted from Ref. [63].

In a scale-free network, the existence of individuals of an arbitrarily large degree implies that there is no level of uniform random vaccination that can prevent an epidemic propagation, even extremely high densities of randomly immunized individuals can prevent a major epidemic outbreak. The discussed susceptibility of these networks to epidemic hinders the implementation of a prevention strategy different from the trivial immunization of all the population [54, 55, 66].

Taking into account the inhomogeneous connectivity properties of scale-free networks can help to develop successful immunization strategies. The obvious choice is to vaccinate individuals according to their connectivity. A selective vaccination can be very efficient, as targeting some of the superspreaders can be sufficient to prevent an epidemic [55, 67].

The vaccination of a small fraction of these individuals increases quite dramatically the global tolerance to infections of the network.

When comparing the uniform and the targeted immunization procedures [67], the results indicate that while uniform immunization does not produce any observable reduction of the infection prevalence, the targeted immunization inhibits the propagation of the infection even at very low immunization levels. These conclusions are particularly relevant when dealing with sexually transmitted diseases, as the number of sexual partners of the individuals follows a distribution pattern close to a power law.

Targeted immunization of the most highly connected individuals [64, 65, 67] proves to be effective, but requires global information about the architecture of network that could be unavailable in many cases. In Ref. [68], the authors proposed a different immunization strategy that does not use information about the degree of the nodes or other global properties of the network but achieves the desired pattern of immunization. The authors called it acquaintance immunization as the targeted individuals are the acquaintances of randomly selected nodes. The procedure consists of choosing a random fraction p_i of the nodes, selecting a random acquaintance per node with whom they are in contact and vaccinating them. The strategy operates at the local level. The fraction p_i may be larger than 1, for a node might be chosen more than once, but the fraction of immunized nodes is always less than 1. This strategy allows for a low vaccination level to achieve the immunization threshold. The procedure is able to indirectly detect the most connected individuals, as they are acquaintances of many nodes so the probability of being chosen for vaccination is higher.

VI. Final remarks

The mathematical modeling of the propagation of infectious diseases transcends the academic interest. Any action pointing to prevent a possible pandemic situation or to optimize the vaccination strategies to achieve critical coverage are the core

of any public health policy. The understanding of the behavior of epidemics showed a sharp improvement during the last century, boosted by the formulation of mathematical models. However, for a long time, many important aspects regarding the epidemic processes remained unexplained or out of the scope of the traditional models. Perhaps, the most important one is the feedback mechanism that develops between the social topology and the advance of an infectious disease. The new types of models developed during the last decade made an important contribution to the field by incorporating a mean of describing the effect of the social pattern. While a quantitative analysis of a real situation still demands huge computational resources, the mathematical foundations to develop it are already laid. The is too much to do yet, but the breakthrough produced by these new models based on complex networks is already undeniable.

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