EPIDEMIC SPREADING AND COMPLEX NETWORKS

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Contents

Summary

The mathematical modeling of epidemics is a very active field of research which crosses different disciplines. Epidemiologists, computer scientists, and social scientists share a common interest in studying spreading phenomena and rely on very similar models for the description of the diffusion of viruses, knowledge, and innovation. Epidemic modeling has developed an impressive array of methods and approaches aimed at describing spreading phenomena, from an abstract point of view to a very detailed modeling of realistic outbreaks, thus widening its theoretical framework to deal with the intrinsic complexity inherent in real situations. In this chapter, we introduce the general framework of epidemic modeling in complex networks at different scales, and show how large heterogeneities affect the basic properties of disease spreading processes.

1. Introduction

A vast array of methods and approaches of increasing complexity have been developed to tackle the understanding of epidemic spreading phenomena (Anderson and May, 1992) (Figure 1). At the simplest level, the compartmental models divide a population into different classes or compartments, depending on the stage of the disease. More refined approaches consider the structure of the population in age or social groups, or the complex properties of the networks of contacts between individuals. In the case of spatially extended systems (Riley, 2007), schemes may explicitly include spatial structures and consist of multiple sub-populations coupled by traveling fluxes, while the epidemic within the sub-population is described according to approximations depending on the specific case studied (Hethcote, 1978; Anderson and May, 1984; May and Anderson, 1984, Bolker and Grenfell, 1993, 1995; Lloyd and May, 1996, Grenfell and Bolker, 1998; Keeling and Rohani, 2002; Ferguson et al, 2003, Rvachev and Longini, 1985; Keeling et al, 2001; Hufnagel et al, 2004; Colizza et al, 2006a,b,2007a,b). At the most detailed level, agent based models (ABM) stretch even more the usual modeling perspective, by simulating the propagation of an infectious disease individual by individual (Chowell et al, 2003; Eubank et al, 2004; Longini et al, 2005, Ferguson et al, 2005, Germann et al, 2006). Clearly, an interplay exists between the simplicity of the model and the accuracy of its predictions.
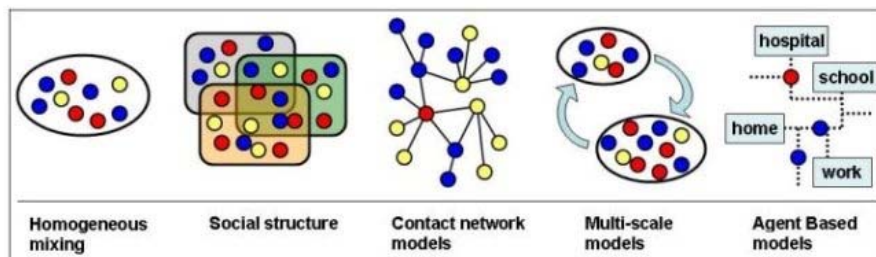

Figure1. Different scales structure used in epidemic modeling. Circles represent individuals and each color corresponds to a specific stage of the disease. From left to right: homogeneous mixing, in which individuals are assumed to homogeneously interact with each other at random; social structure, where people are classified according to demographic information (age, gender, etc.); contact network models, in which the detailed network of social interactions between individuals provide the possible virus propagation paths; multi-scale models which consider sub-population coupled by movements of individuals, while homogeneous mixing is assumed on the lower scale; agent based models which recreate the movements and interactions of any single individual on a very detailed scale (a schematic representation of a city is shown).

The possibility to use the above modeling approaches to understand and forecast epidemic spreading relies on the availability of actual and detailed data on the activity of individuals, their interactions and movement, as well as the spatial structure of the environment, transportation infrastructures, traffic networks, and travel times. While for a long time the access to such data was arduous and extremely limited, the development of new informatics tools and the increase in computer power have enabled in the recent years a tremendous progress in data gathering and analysis (Lazer et al, 2009; Pentland, 2009; Onnela et al, 2007; Brockmann et al, 2006; Watts et al, 2007; Gonzalez et al,

2008). A huge amount of data has become finally available for scientific analysis and study. The scientific community has subsequently uncovered in such data the presence of complex properties and heterogeneities which cannot be neglected in the epidemic modeling description. In particular, the ever increasing level of interconnectedness and globalization of our modern society along with a high level of diversity and heterogeneity induces a novel epidemiological context: the mathematical and computational modeling of disease spread needs to integrate such complex features.

In this context, the recent advances of the field of complex network studies have proven extremely valuable at various levels. The complex properties of individuals interactions and movements find indeed a convenient description in terms of networks (Albert and Barabasi, 200; Dorogotsev and Mendes, 2003; Pastor-Satorras and Vespignani, 2003; Caldarelli, 2007). At the level of a population, the contacts between individuals, through which a virus can propagate, are taking place along social networks. At larger scales, movements of individuals depend on the transportation networks such as e.g. the air transportation networks. They are measured through the travel patterns (at scales ranging from commuting patterns to world-wide travels) and expressed as fluxes of travelers between possible locations, which also find a natural description in terms of travel networks.

In this chapter, we give an overview of how recent advances in network science, the increased computational power and innovative use of Information and Communication Technologies (ICT) have led to new understandings and new frameworks for epidemic modeling, leading to the development of sophisticated modeling approaches informed by realistic and detailed data sets aimed at predicting a variety of possible scenarios, evaluating treatment and control strategies, helping and supporting the decision process at the scientific, medical and public health level.

2. Epidemic Spreading

2.1. Generalities

Basic epidemic models usually start by the definition of the various stages of a disease, and the probabilities for individuals to evolve from one stage to another, possibly by contact and contagion processes between individuals (Anderson and May, 1992). The patterns of contacts between individuals enter therefore as a crucial component in the evolution of the disease. Such patterns have to be characterized both at a local scale, for each individual (do all individuals typically meet the same number of other individuals, or are there strong differences between individuals?), and at the community level (for instance how do people move between locations in a city?). The complex properties of human behaviors might therefore have a strong effect on the epidemic spreading evolution and should be correctly taken into account and integrated into epidemic modeling.

On a global scale, the emergence and spread of infectious diseases has long been known to depend on international travel and commerce (Massey, 1933; Morens, 1998). A striking example is given by the comparison between pre-industrial and recent epidemic spreading patterns. A famous case of pre-industrial outbreak for which it is possible to

obtain extensive historical data is provided by the spread of the so-called Black Death (a bubonic plague) in Europe during the 14th century. At that time, travel was limited in time and space, long range traveling was rare, and it is possible to consider that infected individuals diffused smoothly, generating an epidemic front that travels as a continuous wave through geographical regions. Historical studies confirm that the propagation indeed followed such a simple scheme. In particular, the Black Death spread through Europe from South to North (see Figure 2), with an invasion front moving at an approximate velocity of 200-400 miles/year (Murray, 1993). In modern societies, human traveling fluxes have increased tremendously, and long distances can be covered in short times. This unavoidably leads to new scenarios of epidemic spreading, of which recent examples are given by the SARS and the H1N1 epidemics (Peiris et al, 2003; Balcan et al, 2009a). In both cases, distant countries were affected very rapidly after the emergence of the new virus. Figure 2 (right panel) shows the spatio-temporal pattern of the global SARS spread, with a very rapid and patched structure of the main diffusion with distant outbreaks in Canada and in continental Europe. Understanding this type of spatio-temporal pattern, computing probabilities of diseases outbreak and time lags probabilities are all challenges that modern global epidemiology has to face.

These considerations highlight that, starting from the very simple epidemic models, it is important to introduce complex patterns at various scales. Modern epidemiology faces new challenges in putting together these scales and fully integrating the multiscale complexity of human social contact patterns and flows in the description of the spread of a contagious disease.
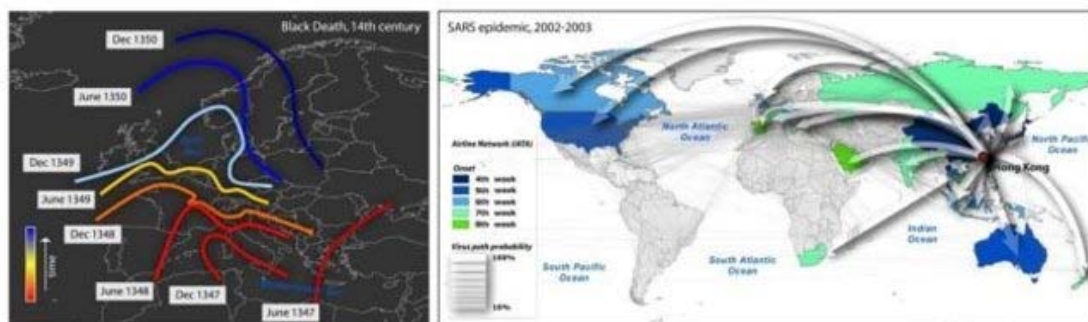

Figure 2. Epidemic spreading pattern changed dramatically after the development of modern transportation systems. In pre-industrial times disease spread was mainly a spatial diffusion phenomenon. During the spread of Black Death in 14thcentury Europe, only few traveling means were available and typical trips were limited to relatively short distances on the time scale of one day. Historical studies confirm that the disease diffused smoothly generating an epidemic front traveling as a continuous wave through the continent at an approximate velocity of 200-400 miles/year. The SARS outbreak on the other hand was characterized by a patched and heterogeneous spatio-temporal pattern mainly due to the air transportation network identified as the major channel of epidemic diffusion and able to connect far apart regions in a short time period. The SARS maps are obtained with a data-driven stochastic computational model aimed at the study of the SARS epidemic pattern and analysis of the accuracy of the model's predictions. Simulation results describe a spatio-temporal evolution of the disease (color coded countries) in agreement with the historical data. Analysis on the robustness of the

model's forecasts leads to the emergence and identification of *epidemic pathways* as the most probable routes of propagation of the disease. Only few preferential channels are selected (arrows; width indicates the probability of propagation along that path) out of the huge number of possible paths the infection could take by following the complex nature of airline connections (light grey, source: IATA).

2.2. Basic Epidemic Modeling: Compartmental Models, the Homogeneous Mixing Assumption and the Epidemic Threshold

In general, epidemic models deal with the evolution of the number and location of infected individuals in the population as a function of time. Their goal is to understand the properties of epidemics both at short times, such as how an outbreak will evolve, and at long times: e.g. will there be a non-zero density of infected individuals, an endemic phase, or a global outbreak? How can non-seasonal cycles emerge and be sustained? In this context, a very important basic parameter is the *basic reproductive number,* usually denoted by R_0. This quantity counts the number of secondary infected cases generated by one primary infected individual in a fully susceptible population. One can intuitively understand that epidemics will spread if, for each infected, the number of new infectious individuals generated by a case while he/she is infected is larger than one, i.e. $R_0 > 1$. In the opposite case, the epidemic outbreak will decay rapidly. This leads to the definition of a crucial concept: the epidemic threshold, which separates epidemics that will affect a finite fraction of the population from outbreaks which die out in a finite time and do not affect strongly the population. The epidemic threshold is a central concept which provides a reference frame and defines a target for containment and mitigation measures, aimed at an effective reduction of the reproductive number below 1 in order to stop the epidemic outbreak. In the following paragraphs, we will define the main basic models of epidemic modeling, show how to derive the epidemic threshold condition in some simple cases, and describe how taking into account complex properties of the interaction networks drastically alters the results.

2.2.1. Definition of the Compartmental Models

In the most basic approach to epidemic modeling, the population is divided into different classes, usually called *compartments,* depending on the stage of the disease. For instance, healthy individuals are classified into the compartment of *susceptible* (denoted by *S*), while individuals who have contracted the infection and are contagious sit in the i*nfectious* (*I*) compartment (Anderson and May, 1992; Murray, 1993). Another often considered compartment encompasses the *recovered* individuals (*R*, who have recovered from the disease and are no more susceptible), and additional compartments may also be used to model, for instance, people immune to the disease, vaccinated individuals, asymptomatic infectious, or individuals exposed to the infection but not yet infectious (exposed, *E*). In this simple framework, the stages of the disease are therefore discretized into the different compartments. Moreover, individuals differ only through their infection stage, and are assumed to be identical and homogeneously mixed within each compartment.

The division into compartments is complemented by the definition of the rules which

govern the transitions of individuals from one compartment to another, and which depend on the disease etiology. In general, two classes of processes can be distinguished. The simplest class corresponds to spontaneous transitions of one individual from one compartment to another. Examples include the spontaneous recovery of infected individual ($I \rightarrow R$), or the evolution from a latent to an infectious state after the incubation period ($E \rightarrow I$). The second class corresponds to contagion processes, i.e. binary interactions, such as the contagion of a susceptible individual by an infectious one (represented by: $S + I \rightarrow 2I$).

Using this general framework, one can derive the dynamical equations which describe the evolution of the number of individuals in each compartment. We will here consider the three basic models commonly used to illustrate and explore the properties of epidemic spreading phenomena (Anderson and May, 1992; Murray, 1993). The simplest one, the susceptible-infected (SI) model considers that individuals are either susceptible or infectious, and individuals who become infected by contact with an infectious remain forever in this compartment. In the susceptible-infected-susceptible (SIS) model in contrast, infectious individuals become spontaneously susceptible again, while in the susceptible-infected-recovered (SIR) model, infectious individuals recover spontaneously, but enter the recovered compartment and cannot be infected again.

Let us first consider the SI model. In this case, the number of infectious individuals can only increase, and the population is ultimately entirely affected. The evolution of the model as a function of time *t* is entirely described by the number of infected individuals $I(t)$ or equivalently the corresponding density $i(t) = I(t) / N$ in a population of N individuals. The number $S(t)$ of susceptible is simply given by the conservation of the total number $N = S(t) + I(t)$.

Denoting by β the pathogen *transmission rate per contact*, the probability that a susceptible individual acquires the infection from an infectious contact in a small time interval dt is by definition βdt. The force of infection (the per capita rate of acquisition of the disease) for a susceptible will therefore be given by the transmission rate per contact β and his/her number of contacts with infectious individuals.

If we assume homogeneous mixing in the population, the number of contacts with infectious individuals will be simply given by the number of contacts k times the probability to find an infectious individual in the population, given by the density $i(t)$. This corresponds to assuming that each individual has the same number of contacts $k \sim <k>$, and that the contact with a specific class is determined only by the incidence of that class in the population, i.e. individuals mix homogeneously. Therefore, the evolution of the SI model is described by the following deterministic reaction rate:

$$\frac{di}{dt} = \beta \langle k \rangle i(t) [1 - i(t)].$$

This equation states that the growth of the density of infected individuals is proportional to the spreading rate $\beta <k>$, the density $1-i(t)$ of susceptible that may become infected, and the number of infected individuals in contact with any susceptible individual.

In the SIS and SIR models, the disease transmission is described as in the SI model, while the probability of spontaneous recovery of each infected individual is μdt, where μ is the r*ecovery rate*. For the SIS case, the individuals become susceptible again and may thus be re-infected, going through the cycle susceptible $\rightarrow$ infected $\rightarrow$ susceptible. Since individuals can be only in one of two states, the state of the population is once again fully described by the density of infected, whose evolution is described by the equation

$$\frac{di}{dt} = -\mu i(t) + \beta \langle k \rangle i(t)\left[1 - i(t)\right].$$

In the SIR case, the infected individuals who recover enter a new compartment R, whose density is denoted by $r(t) = R(t)/N$. The evolution of the epidemics is then described by two variables, for instance $i(t)$ and $r(t)$, and the number of susceptible is given by the conservation equation $S(t) + I(t) + R(t) = N$. The processes of contamination and recovery are described as in the SIS model, so that the evolution equations read

$$\frac{di}{dt} = -\mu i(t) + \beta \langle k \rangle i(t)\left[1 - r(t) - i(t)\right].$$
$$\frac{dr}{dt} = \mu i(t).$$

Clearly, the dynamical rules of the SIR model imply that any infected individual becomes recovered at some point, so that at large time the epidemic necessarily disappears.

The dynamical evolution of both SIS and SIR models show that two time scales appear and compete in the spreading process: the spontaneous recovery of individuals occur on a time scale $1/\mu$, while the spreading time scale is given by $1/\beta <k>$. Let us first consider the limiting case in which $1/\mu$ is much smaller than $1/\beta <k>$. It is then intuitively clear that the process will be dominated by the recovery of infected individuals towards the susceptible or the recovered compartments. In this case, the epidemic outbreak will not spread. In contrast, it the spreading time is much smaller than the recovery time ($1/\mu$ much larger than $1/\beta <k>$), the recovery process can be neglected in a first approximation for the study of the early dynamics of the epidemic outbreak. This corresponds to the SI model, and therefore in this limit the infection will affect a large proportion of the population. These two limiting cases define two different

regions in the parameters space which result in very different behaviors of the spreading process, and a transition from one regime to the other must occur at a certain value of the parameters, as we will see in the next paragraph.

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