Chapter 27

Social Networks, Contagion Processes and the Spreading of Infectious Diseases

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INTRODUCTION

The characterization and understanding of contagion phenomena is crucially dependent upon the conceptual framework adopted to describe groups of individuals (social agents) or entire populations in spatially extended systems, and of the interaction and behavior of individuals at various levels, from the global scale of mobility and transportation flows to the local scale of individual activities and contacts. In this context, a mathematical and statistical modeling framework has evolved from simple compartmental models into structured approaches in which the heterogeneities and details of the population and system under study are becoming increasingly important (Figure 27.1). In the case of spatially extended systems, modeling approaches have been extended into schemes that explicitly include spatial structures and which consist of multiple subpopulations coupled by traveling fluxes, while the epidemic within the subpopulation is described according to approximations depending on the specific case studied [1–9]. This patch or metapopulation modeling framework has then grown into a multi-scale framework in which the various possible granularities of the system (country, inter-city, intra-city) are considered through different approximations and coupled through interaction networks describing the flows of people and/or animals [9–16]. At the most detailed level, the introduction of agent-based models (ABM) has enabled us to stretch the usual modeling perspective even more to achieve a full description of the society by a complete characterization (household, workplace, etc.) of each individual [17,18].

The above modeling approaches are 'data hungry', as they depend on detailed information about the activity of individuals, their interactions and movement, as well as the spatial structure of the environment, transportation infrastructures, traffic networks, and travel times. Although for a long time these kinds of data were simply not available, recent years have witnessed a tremendous progress in data gathering thanks to the development of new informatics tools and the increase in computational power. A continuous flow of data has finally become available for scientific analysis and study. The availability of data has allowed highlighting of complex properties and heterogeneities, which cannot be neglected in the epidemic description. Although these characteristics have long been acknowledged as a relevant factor in determining the properties of dynamical processes, many real-world networks exhibit levels of heterogeneity that were not anticipated until a few years ago, and represent a theoretical and conceptual challenge in our understanding of the unfolding of contagion processes.

Although data availability is highlighting the limits of our conceptual and modeling frameworks, it is also allowing the validation of results across different modeling approaches, mathematical techniques and approximation schemes. Furthermore, it has been possible to push forward the development of data-driven computational approaches

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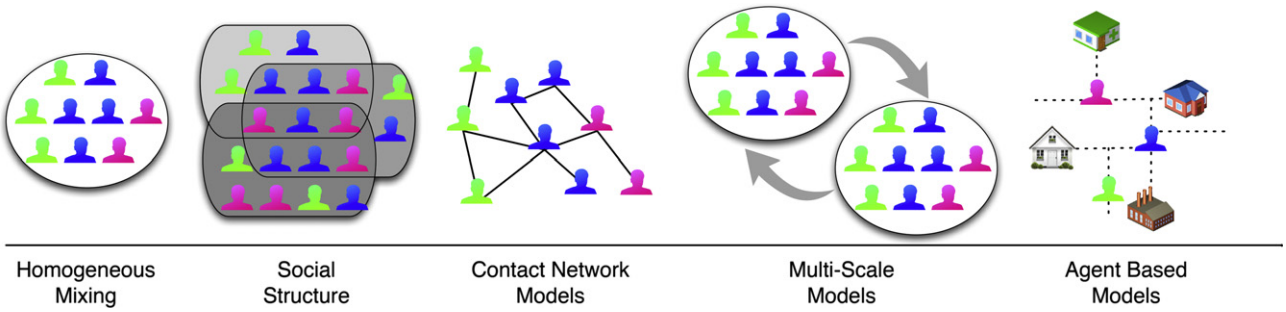


FIGURE 27.1 Different scale structures used in epidemic modeling. Circles represent individuals and each color corresponds to a specific stage of the disease. From left to right: homogeneous mixing, in which individuals are assumed to interact homogeneously with each other at random; social structure, 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 subpopulation 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).

based on the construction of highly detailed synthetic societies. Within such a framework computer simulations acquire a new value and allow on the one hand the creation of in silico experiment hardly feasible in real systems, and access to quantity and observables across different models on the other. This computational thinking approach will be also the guide to the understanding of typical non-linear behavior and tipping points not accessible by analytical means.

Although many basic conceptual questions remain unresolved, the major challenge in the development of models able to capture the behavior of large-scale techno-social systems is their sensitivity and dependence on social adaptive behavior. In the absence of a stress on the system, a stationary state is reached in which the feedback between the social behavior and the environment determines the details of how the dynamical process of interest plays out. Social behaviors react, adapt and define new way of interacting as the dynamics of the system evolves. This complicates the problem tremendously and clearly shows the limits in our understanding of human behavior. The view we have of human mobility, for example, is the daily normal activity of individuals. In the case of a major event, such as the spread of a novel pandemic, all the techno-social systems we are part of can be pushed out of equilibrium. Under stress individuals can act differently from usual: they can decide to stay home, to avoid crowded places and prevent children attending school. In general, they can take any action to reduce their risk by self-initiated behavioral changes. Contrary to what happens in physical systems, the global evolution of the system and our knowledge of it are part of the system dynamic.

Unfortunately, we are still not able to capture and deeply understand social adaptation and quantify the consequent changes on the dynamics of processes that trigger it. While some of the above issues may find a partial solution by improving the accuracy and reliability of models, it is clear that social adaptation to predictions presents us with new methodological and ethical problems.

Addressing these problems involves tackling three major scientific challenges. The first is the gathering of large-scale data on information spread and social reactions. This is not currently out of reach, thanks to large-scale mobile communication databases (mobile telephone, Twitter logs, social web tools) operating at times of specific disaster or crisis events. Second is the formulation of formal models that make it possible to quantify the adaptation, changes and reactions of individuals as a function of the dynamic processes occurring in the system. The third challenge concerns the deployment of monitoring infrastructures capable of informing computational models in real time.

NETWORK THINKING

The study of contagion processes is a very active field of research that 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 [19–23]. All these processes define a contagion dynamic, which can be an actual biological pathogen that spreads from host to host, or a piece of information/knowledge that is transmitted during social interactions. The connectivity patterns describing the interactions of individuals as well as their mobility from place to place are one of the crucial ingredients in the understanding of contagion phenomena. The importance of networks in epidemiology need not be stressed here. The recent advances in the field, however, stem from the increased ability to gather data on several large sets of networked structures and populations. For a long time approaches to human interactions and mobility have relied mostly on census and survey data on social interactions,

frequently incomplete and/or limited to a specific context. A multitude of heuristic models for population structure and mobility (e.g., gravity laws of various types) have been endorsed, yet they frequently generate conflicting results and all suffer from the shortcomings of being connected to the arbitrariness of administrative boundaries, lacking microscopic knowledge relating the individual dynamics to population interactions, and lacking network and spatial proximity correlations. Put simply, despite the large effort and relevant advances in the study of human transport, no general framework of human interactions and mobility based on microdynamic principles and able to bridge all spatial scales exists. The new era of the social web and the data deluge is, however, raising the limits scientists have long been struggling with. From the development of new pervasive technologies to the use of proxy data, such as the digital traces that individuals leave with their mobile devices, it is nowadays possible to characterize the network of human interactions from the scale of the single individual to the level of entire populations.

The first steps towards a cohesive framework for the collection of detailed data on human behavior and mobility started by passively tracking human interactions through the use of cell phones [24]. Each cell phone was equipped with custom software that would regularly check which cell phone towers and Bluetooth devices were within range. Since Bluetooth has a range that is limited to just a few meters, they were able to track the location of each user with a hitherto unprecedented resolution up to room level. This pioneering study introduced the concept of 'reality mining', the idea that technology had finally reached a point where it was not only feasible but also easy to unobtrusively track individual behavior and social interactions in real time. What followed was an avalanche of works extending this approach in various directions, both by using pre-existing data in innovative ways and by creating new tools and techniques to obtain data that had never been available before. Similar experiments have been used recently to generate predictive power on influenza spreading in communities by mapping the social pattern of individuals along with their health status [25].

Analogous experiments are also performed with progressively smaller, lightweight, active Radio-Frequency Identification (RFID) tags [26]. Each tag emits a low-power directed radio signal with a range of up to 1 m. Whenever two tags are able to exchange signals for an extended period of time, this is a clear sign that the people wearing them are facing each other and in close proximity, providing a good indication that a face-to-face conversation is taking place. The authors distributed such tags to hundreds of volunteers in various settings, and for the first time were able to track the way in which face-to-face interactions occur in real-world settings ranging from school and hospitals to conferences and workplaces.

In a pioneering work, Dirk Brockmann and co-workers have shown that popular sites for currency tracking (eurobilltracker, wheresgeorge) can be used to gather a massive number of records on money dispersal, and to use those as a proxy on humans to collect a wealth of novel and unprecedented data. This work opens a novel path to the general exploitation of proxy data for human interaction and mobility based on the evidence that humans leave abundant traces of their interactions and mobility patterns within various types of data-driven websites. The pervasive use of mobile and Wi-Fi technologies in our daily life is also changing the way we can measure human mobility. Modern mobile phones and PDAs combine sophisticate technologies such as Bluetooth, GPS, and WiFi, constantly producing detailed traces of our daily activities. The recent study of Gonzalez and co-workers on human mobility based on mobile phone data to track the movements of 100 000 people over 6 months is just the most explosive example of how these kinds of data are going to shatter our methodology in the field and critically revise our knowledge of social dynamics.

One of the main challenges offered by these networks lies in their complexity and multi-scale nature. As a large body of work spurred by first paper on complex networks has shown, most real-world networks present dynamical self-organization and the lack of characteristic scales, main hallmarks for complex systems. The various statistical distributions characterizing these networks are generally heavy-tailed, skewed and varying over several orders of magnitude. This is not just true for the degree distribution $P(k)$ characterizing the probability that each node in the system is connected to k neighboring nodes, it is observed for the intensity carried by the connecting links, transport flows and other basic quantities.

Analogously, similar heterogeneities are found at much larger resolution scale. At the urban scale of a single city, an impressive characterization of the human interactions flows is represented by the TRANSIM study [17]. This study focused on the network of locations in the city of Portland, Oregon, including homes, offices, shops and recreational areas. The temporal links between locations represent the flow of individuals going from one place to another at a given time. The resulting network is characterized by broad distributions of the degrees and of the flows of individuals traveling on a given connection [17]. Strong heterogeneities are thus present not only at the topological level, but also at the level of the traffic on the network: a simultaneous characterization of the system in terms both of topology and weights associated to connections is needed to integrate the different levels of complexity in a unifying picture [27].

Similar results have been found in commuting patterns among cities and counties within a given geographical region/country. In this case, the nodes of the network

represent cities, counties and in general municipalities or urban aggregations coupled by connections that correspond to the commuting flows of individuals. The analysis of these networks uncovered rather homogeneous topologies — mainly due to strong spatial constraints — associated with very large fluctuations in individuals' travel flows [28].

Finally, the most global scale is characterized by the air connections infrastructure, composed of airports (nodes) and direct flights among them (links). Data representing the travel flow of passengers defines the weight to each connection [27]. This transportation network displays several strong levels of heterogeneity. The distribution of degrees (i.e., of the number of connections of an airport) is scale free and the traffic is very broadly distributed, varying over several orders of magnitude [27,29]. This points to a structure composed of airports having large fluctuations in their number of connections to other airports and, moreover, to the number of passengers traveling on a given route, ranging from a few to millions of individuals in a given period of time.

Figure 27.2 shows two networks for human mobility at different scales ranging from the airline transportation network at the distance of hundreds and thousands of kilometers and several days to the commuting network that connects neighboring cities within the span of a few hours. We see that the scale and complexity extend at all granularities, creating a huge multi-scale network where the time and spatial separations range from a few hundred meters and a few minutes to thousands of kilometers and several days.

The challenge in providing a holistic description of multi-scale networks is the necessity of dealing with multiple time and length scales simultaneously. The final system's dynamical behavior at any scale is the product of the events taking place on all scales. The single agent spreading a disease or single node is apparently not affected by the multi-scale nature of the network, just as single molecules or fluid elements do not care about the multi-scale nature of turbulent fluid. However, the collective dynamic behavior and our ability to conduct mathematical/computational analyses of techno-social systems are constrained by the heterogeneous and multi-scale characteristic of the system, and we must develop appropriate formalisms and techniques, as have done researchers studying multi-scale physical systems [30] (fluids, solids, distribution of masses in the universe, etc.). In the context of networks and techno-social systems, the multi-scale challenge is making its appearance now because of the availability of large-scale datasets. To achieve analytical understanding of techno-social systems and approach them computationally, we must find different strategies to deal with dynamical behavior/equations that work at very different characteristic scales but still influence each other.

CONTAGION PHENOMENA IN COMPLEX SOCIAL NETWORKS

Contagion processes are usually seen as a transmission process, either as a pathogen that spreads from host to host, or a piece of information/knowledge that is transmitted during social interactions. Let us consider the simple susceptible—infected—recovered (SIR) epidemic model. In this model, infected individuals (labeled with the state I) can propagate the contagion to susceptible neighbors (labeled with the state S) with rate λ, while infected individuals recover with rate μ and become removed from the population. This is the prototypical model for infectious disease spreading, where individuals recover and are immune to disease after a typical time that on average can be expressed as the inverse of the recovery rate. A classic variation of this model is the susceptible—infected—susceptible (SIS) model, in which individuals go

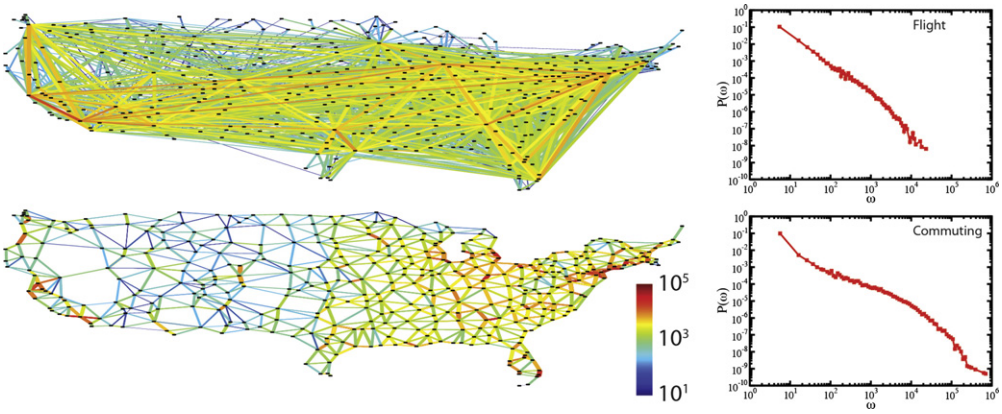


FIGURE 27.2 Multiscale structure of human mobility. (Left) The flight network (top) involves typical periods of several days, whereas the commuting flows (below) occur within a single day but are typically much more intense. (Right) The weight distribution of the flight and commuting networks.

back to the susceptible state with rate μ, modeling the possibility of reinfection.

A cornerstone of epidemic processes is the presence of the so-called epidemic threshold [19]. In a fully homogeneous population the behavior of the SIR model is controlled by the reproductive number $R_0 = \beta/\mu$, where $\beta=\lambda\langle k\rangle$ is the per-capita spreading rate, which takes into account the average number of contacts k of each individual. The reproductive number simply identifies the average number of secondary cases generated by a primary case in an entirely susceptible population and defines the epidemic threshold such that only if $R_0 \geq 1$ ($\beta \varepsilon \mu$) can epidemics reach an endemic state and spread into a closed population. The SIS and SIR models are indeed characterized by a threshold defining a transition between two very different regimes. These regimes are determined by the values of the disease parameters, and characterized by the global parameter i_∞ which identifies the density of infected individuals (nodes in a network) in the infinite time limit. In the limit of an infinitely large population, this density is zero below the threshold and assumes a finite value above the threshold. In this perspective we can consider the epidemic threshold as the tipping point of the system. Below the critical point the system relaxes into a frozen state with null dynamics – the healthy phase. Above this point, a dynamical state characterized by a macroscopic number of infected individuals sets in, defining an infected phase (Figure 27.3).

The above results are generally obtained by using the so-called homogenous assumption in which all individuals in the populations are considered statistically equivalent and no structure (spatiotemporal, connectivity pattern, etc.) is included in the system description.

One of the most important features affecting dynamical processes in real-world networks, however, is the presence

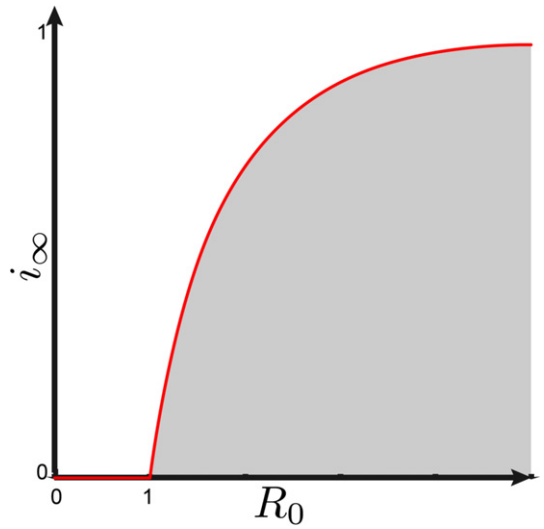


FIGURE 27.3 Phase diagram. Above $R_0 = 1$ the total number of infected individuals becomes a finite fraction of the population size.

of dynamic self-organization and the lack of characteristic scales – typical hallmarks of complex systems [31–35]. In particular, the various statistical distributions characterizing social networks are generally heavy-tailed, skewed, and varying over several orders of magnitude. This is a very peculiar feature typical of many natural and artificial complex networks, characterized by virtually infinite degree fluctuations, where the degree k of a given node represents its number of connections to other nodes. In contrast to regular lattices and homogeneous graphs characterized by nodes having a typical degree k close to the average $\langle k\rangle$, such networks are structured in a hierarchy of nodes, with a few nodes having very large connectivity – the hubs – while the vast majority of nodes have smaller degrees (see Chapter 9). This feature usually finds its signature in a heavy-tailed degree distribution, often approximated by a power-law behavior of the form $P(k) \propto x^{-\gamma}$, which implies a non-negligible probability of finding vertices with very large degree [32–35].

The presence of large-scale fluctuations virtually acting at all scales of the network connectivity pattern calls for a mathematical analysis where the variables characterizing each node of the network are explicitly entering the description of the system. Unfortunately, the general solution, handling the master equation of the system, is hardly if ever achievable even for very simple dynamical processes. For this reason, a viable theoretical approach considers the use of techniques such as mean-field and deterministic continuum approximations, which usually provide the understanding of the basic phenomenology and phase diagram of the process under study. In both cases the heterogeneous nature of the network connectivity pattern is introduced by aggregating variables according to a degree block formalism which assumes that all nodes with the same degree k are statistically equivalent [36–38]. This assumption allows the grouping of nodes in degree classes, yielding a convenient representation of the system. For instance, if for each node i we associate a corresponding state σ_i characterizing its dynamical state, a convenient representation of the system is provided by the quantities S_k that indicates the number of nodes of degree k in the dynamical state $\sigma = s$ and the corresponding degree block density of nodes of degree k in the state s

$$s_k = \frac{S_k}{V_k}$$

where V_k is the number of nodes of degree k. Finally the global averages on the network are then given by the expressions

$$\rho_s = \sum_k P(k) s_k$$

where ρ_s is the probability that any given node is in the state s. This formalism is extremely convenient in networks

where the connectivity pattern dominates the system's behavior as the above degree block variables define a mean-field approximation within each degree class, relaxing however the overall homogeneity assumption on the degree distribution [38]. This framework, first introduced for the description of epidemic processes, is the basis of the heterogeneous mean-field (HMF) approach which allows the analytical study of dynamical processes in complex networks by writing mean-field dynamical equations for each degree class variable. The HMF approach generalizes to the case of networks with arbitrary degree distribution the equations describing the dynamical process by considering degree block variables grouping nodes within the same degree class k. If we consider the SIS model, the variables describing the system are i_k, s_k and r_k that represent the fraction of nodes with degree k in the susceptible, infected and recovered class. The evolution equation for the infected individual reads as

$$\frac{di_k(t)}{dt} = -\mu i_k(t) + \lambda[1 - i_k(t)]k\Theta_k(t)$$

Here the first term simply expresses the fact that any node in the infected state may recover with rate μ. The second term, which generates new infected individuals, is proportional to the probability of transmission λ, the degree k, the probability $1\text{-}i_k$ that a vertex with degree k is not infected, and the density Θ_k of infected neighbors of vertices of degree k, i.e., the probability of contacting an infected individual. As we are still assuming a mean-field description of the system, the latter term is the average probability that any given neighbor of a vertex of degree k is infected. This quantity can be expressed as $\Theta_k(t) = P(k'|k)i_{k'}(t)$, which considers the average over all possible degrees k' of the probability $P(k'|k)$ that any edge of a node of degree k is pointing to a node of degree k' times the probability $i_{k'}$ that the node is infected. This expression can be further simplified by considering a random network in which the conditional probability does not depend on the originating node. In this case we have that $P(k'|k) = k'P(k')/<k>$ simply descending from the fact that any edge has a probability to point to a node with degree k' which is proportional to the degree itself [38].

The HMF technique is often the first line of attack in understanding the effects of complex connectivity patterns on dynamical processes and has been widely used in a wide range of phenomena, although with different names and specific assumptions depending on the problem at hand. Although it contains several approximations, the HMF approach readily shows that the heterogeneity found in the connectivity pattern of many networks may drastically affect the unfolding of the dynamical process, providing novel and interesting features that depart from the common picture we are used to in regular lattices and homogenous population.

The classic example of the effect of degree heterogeneity on dynamical processes in complex networks is offered by epidemic spreading. The previously discussed result of the presence of an epidemic threshold in the SIR and SIS models is obtained under the assumption that each individual in the system has, at a first approximation, the same number of connections $k \cong <k>$. However, social heterogeneity and the existence of 'super-spreaders' have long been known in the epidemics literature [39]. Generally, it is possible to show that the reproductive rate R_0 is re-normalized by fluctuations in the transmissibility or contact pattern as $R_0 \rightarrow R_0(1 + f(\upsilon))$, where $f(\upsilon)$ is a positive and increasing function of the standard deviation ν of the individual transmissibility or connectivity pattern [40]. In particular, by generalizing the dynamical equations of the SIS model, the HMF approach yields that the disease will affect a finite fraction of the population only if $\frac{\beta}{\mu} \geq <k>^2 / <k^2>$ [36,38]. This readily points out that the topology of the network enters the very definition of the epidemic threshold through the ratio between the first and second moments of the degree distribution. Furthermore, this implies that in heavy-tailed networks such that $<k^2> \rightarrow \infty$, in the limit of a network of infinite size, we have *a null epidemic threshold*. While this is not the case in any finite size real-world network [41,42], larger heterogeneity levels lead to smaller epidemic thresholds (see Figure 27.3). This is a very relevant result indicating that heterogeneous networks behave very differently from homogeneous networks with respect to physical and dynamical processes. Indeed, the heterogeneous connectivity pattern of networks also affects the dynamical progression of the epidemic process, resulting in striking hierarchical dynamics in which the infection propagates from higher to lower degree classes. The infection first takes control of the large degree vertices in the network, then rapidly invades the network via a cascade through progressively smaller degree classes (Figure 27.4). It also turns out that the time behavior of epidemic outbreaks and the growth of the number of infected individuals are governed by a time scale τ proportional to the ratio between the first and second moments of the network's degree distribution, thus pointing to a velocity of progression that is increasing with the heterogeneity of the network [43].

The change of framework induced by the network heterogeneity in the case of epidemic processes has triggered a large number of studies aimed at providing more rigorous analytical basis to the results obtained with the HMF and other approximate methods, and exploring different spreading models [44–48]. In particular, the HMF approach is exact for networks whose connections are fixed only on average, annealed networks. For networks that instead have fix connections, quenched networks, the HMF approach does not always give correct results and interpretations. Indeed, in these networks there are striking

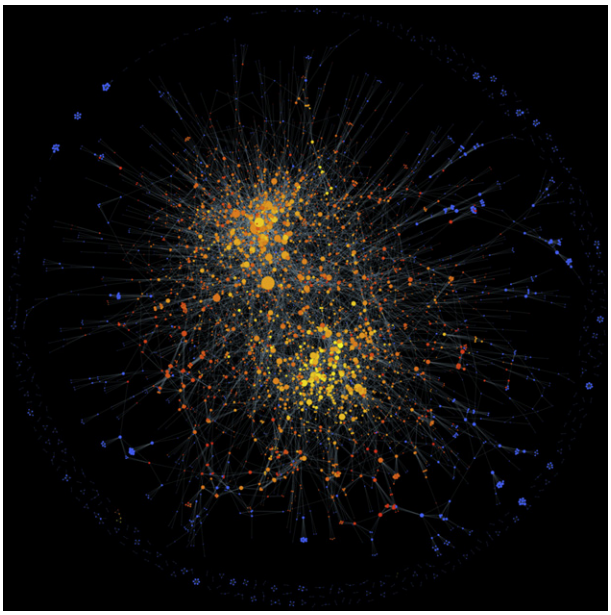


FIGURE 27.4 Epidemic progression in a scale-free network. Node size represents the degree and the color varies between yellow and red to indicate the time of infection. Blue nodes are never infected and remain susceptible.

differences between the results for SIR and SIS models [21]. While the SIR model results are in good agreement with the HMF theory also in quenched networks, the SIS model results can be completely different from those predicted by the HMF. Exact solutions have recently shown that quenched networks characterized by a maximum degree that diverges with the system size, always have a zero threshold [21,49]. In other words, the threshold of a SIS model is zero also for networks of finite second moment if the largest degree is a growing function of the network size, contrary to the indications of the HMF theory. The reasons behind the differences between the SIR and SIS models in this context are not really clear and are still a matter of debate, but are probably related to the absence/existence of a steady state of infected individuals [21].

Heterogeneous networks are extremely permeable epidemics attacks [38,50] and at the same time uniform immunizations are clearly not effective in this type of network. They give the same importance to very connected nodes and to nodes with very few connections, which instead have completely different roles in the spreading of the epidemic. The introduction of fraction g of nodes immune to the disease, immunized, is equivalent to a simple rescaling of the per capita spreading rate that becomes

$$\frac{\beta}{\mu} = \frac{<k>^2}{<k^2>}\frac{1}{(1-g)}$$

The change in the parameter is just proportional to the fraction of nodes not immunized. For a SIR model at the HMF level we have a vanishing threshold, implying that for power-law networks characterized by a divergent second moment of the degree distribution the disease will always spread except when $g = 1$ [38]. For finite networks this fraction is < 1 but still close to this value. It is then extremely relevant to research activity concerning the developing of dynamical ad-hoc strategies for network protection: targeted immunization strategies and targeted prophylaxis that evolve with time might be particularly effective in the control of epidemics on heterogeneous patterns, compared to massive uniform vaccinations or stationary interventions [51–54].

For instance, nodes with high degree are the ones more likely to spread the disease. Immunizing them through a targeted scheme is the most efficient way to protect the network from the disease. Analytical evaluation confirmed by numerical simulations shows that in heterogeneous networks targeted schemes allow complete protection from the disease at the cost of immunizing $<10\%$ of the nodes [38,51].

Although targeted immunization strategies are extremely powerful they rely on a complete knowledge of the network structure. Unfortunately, in most real cases this is partial and limited. To overcome this problem several methods based on local exploration mechanisms have been proposed [51,53,55–57].

In one of the most ingenious strategies a fraction of nodes is selected at random and each one of them is asked to point to one of its neighbors. Each of these neighbors is then immunized. This strategy is based on the heterogeneity of the systems. In these types of networks following links at random gives a higher probability of reaching high degree nodes that have many links pointing to them [56]. This property is often cited as ‘the friendship paradox’, which states that your friends have more friends than you do [35,38].

Many others variation involving chained versions of the previous strategy [57], shortest-path of different sizes [58], and other propagation properties have been proposed [59]. It is important to stress that all of them are based on the heterogeneous features of the network structure.

COMPLEX NETWORKS AND THE LARGE-SCALE SPREADING OF INFECTIOUS DISEASES

The network mindset is necessary not only in describing the connectivity pattern of single individuals in a population. A simple example is provided by the large-scale description of epidemic spreading. The spread of the plague epidemic in the 14th century (the ‘Black Death’) [60] was mainly a spatial diffusion phenomenon. Historical studies have established that disease propagation followed a simple

pattern that can be adequately described mathematically within the framework of continuous differential equations using terms that describe diffusion. As anticipated in 1933 [27], the large scale and geographical impact of infectious diseases (such as the SARS epidemic [29] or the recent swine flu epidemic) on populations in the modern world is mainly due to commercial air travel. An epidemic starting in Mexico rapidly reaches Europe and Asia (Figure 27.5). This picture cannot be simply described in terms of diffusive phenomena, but must incorporate the spatial structure of modern transportation networks.

The conceptual framework to approach spatially structured population is the patch or meta-population modeling framework that considers multiple subpopulations coupled by movements of individuals. These models are defined by the network describing the coupling among the populations along with the intensity of the coupling, which in general represents the rate of exchange of individuals between two populations. Networks are also, in this case, the underlying substrate for the diffusion process. Meta-population models can be devised at various granularity levels (country, inter-city, intra-city) and the corresponding networks therefore include very different systems and infrastructures. This implies scales ranging from the movement of people within locations of a city to the large flows of travelers among urban areas.

At the formal level meta-population models fall into the category of reaction−diffusion processes, where each node i is allowed to have any non-negative integer number of particles N_i so that the total particle population of the system is $N = \sum_i N_i$. In this case particle network frameworks extend the HMF approach to the case of reaction−diffusion systems in which particles (individuals) diffuse on a network with arbitrary topology. A convenient representation of the system is therefore provided by the quantities defined in terms of the degree k

$$N_k = \frac{1}{V_k} \sum_{i|k_i=k} N_i$$

where V_k is the number of nodes with degree k and the sums run over all nodes i having degree k_i equal to k. The variable degree block variable N_k represents the average number of particles in nodes with the degree k. The use of the HMF approach amounts to the assumption that nodes with degree k, and hence the particles in those nodes, are statistically equivalent. In this approximation the dynamics of particles randomly diffusing on the network is given by a mean-field dynamical equation expressing the variation in time of the particle subpopulations $N_k(t)$ in each degree block k. This can easily be written as:

$$\frac{dN_k(t)}{dt} = -d_k N_k(t) + k \sum_k P(k'|k) d_{k'k} N_{k'}(t)$$

The first rhs term of the equation just considers that only a fraction of particles d_k moves out of the node per unit time. The second term instead accounts for the particles diffusing from the neighbors into the node of degree k. This term is proportional to the number of links k times the average number of particles coming from each neighbors. This is equal to average over all possible degrees k' the fraction of particles moving on that edge $d_{k'k}N_{k'}(t)$ according to the conditional probability $P(k'|k)$ that an edge belonging to a node of degree k is pointing to a node of degree k'. Here the term $d_{k'k}$ is the diffusion rate along the edges connecting nodes of degree k and k'. The rate at which individuals leave a subpopulation with degree k is then given by $d_k = k\sum_{k'} P(k'|k) d_{kk'}$. The function $P(k'|k)$ encodes the topological connectivity properties of the network and allows study of the different topologies and mixing patterns. The above equation explicitly brings the diffusion of particles into the description of the system. The equation can be simply generalized to particles with different states and reacting among them by adding a reaction term to the above equations. For instance the generalization of the SIR model described in the text would consider three types of particles denoting infected, susceptible and recovered individuals. The reaction term that would take place among individuals in the same node would be the usual contagion process among susceptible and infected individuals and the spontaneous recovery of infected individuals.

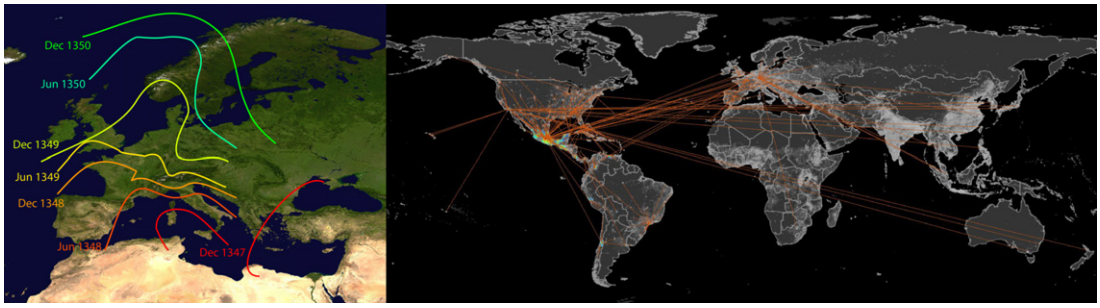


FIGURE 27.5 Historical and modern epidemics. (Left) Map of the propagation of the Black Death in the 14th century. The epidemic front spread in Europe with a velocity of 200−400 miles per year. (Right) Epidemic tree of the first 120 days of the 2009 H1N1 pandemic.

The analysis of a simple diffusion process immediately highlights the importance of network topology. In a random network with arbitrary degree distribution the stationary state reached by a swarm of particles diffusing with the same diffusive rate yields $N_k \propto k$ and the probability of finding a single diffusing walker in a node of degree k is

$$p_k = \frac{k}{<k>}\frac{1}{V}$$

where V is the total number of nodes in the network. This expression tell us that the larger the degree of the nodes, the larger the probability of being visited by the walker. Evidently, the topology of the system has a large impact in the way contagion processes will spread in large meta-population networks.

Consider, for instance, a simple epidemic process such as the SIR model in a meta-population context [56,61–68]. In this case each node of the network is a subpopulation (ideally an urban area) connected by a transportation system (the edges of the network) that allows individuals to move from one subpopulation to another (Figure 27.6). If we assume a diffusion rate d for each individual, and that the single population reproductive number of the SIR model is $R_0>1$, we can easily identify two different limits. If $d=0$ any epidemic occurring in a given subpopulation will remain confined: no individual could travel to a different subpopulation and spread the infection across the system. In the limit $d=1$ we have individuals constantly wandering from one subpopulation to the other and the system is in practice equivalent to a well-mixed single population. In this case, since $R_0>1$, the epidemic will spread across the entire system. A transition point between these two regimes is therefore occurring at a threshold value d_c of the diffusion rate, identifying a global invasion threshold. Interestingly, this threshold cannot be uncovered by continuous models as it is related to the stochastic diffusion rate of single individuals. Furthermore, the global invasion threshold is affected by the topological fluctuations of the meta-population network. In particular, the larger the network heterogeneity, the smaller the value of the diffusion rate above which the epidemic may globally invade the meta-population system. This result assumes

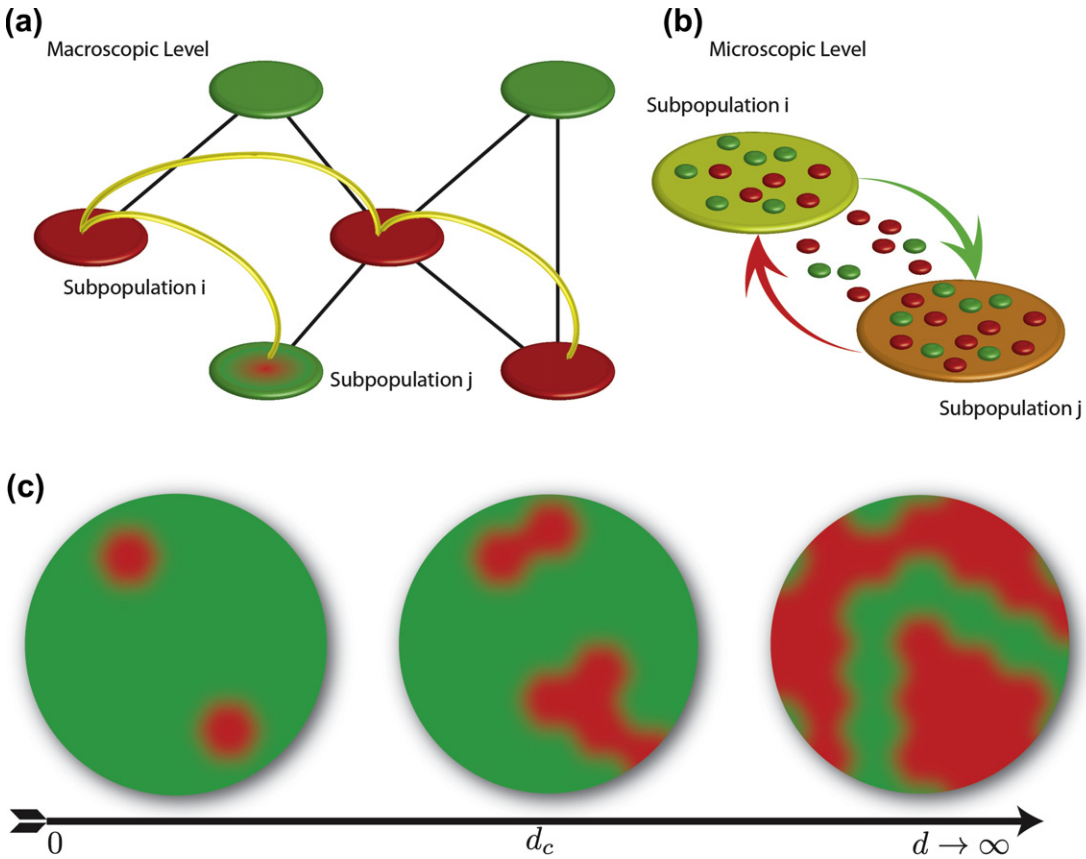


FIGURE 27.6 Illustration of the global threshold in reaction–diffusion processes. (a) Schematic of the simplified modeling framework based on the particle-network scheme. (b) Within each subpopulation individuals can mix homogeneously or according to a subnetwork, and can diffuse with rate d from one subpopulation to another, following the edges of the network. (c) A critical value d_c of the diffusion strength for individuals or particles identifies a phase transition between a regime in which the contagion affects a large fraction of the system and one in which only a small fraction is affected.

a particular relevance as it explains why travel restrictions appear to be highly ineffective in containing epidemics: the complexity and heterogeneity of the current human mobility network favor considerably the global spreading of infectious diseases, and only unfeasible mobility restrictions that reduce the global travel fluxes 90% or more would be effective [57,64,69].

Reaction–diffusion models lend themselves to the implementation of large-scale computer simulations (Monte Carlo and individual-based simulations) that allow microscopic tracking of the state of each node and the evolution of the dynamical process. For instance, state of the art data-driven meta-population models combine highly detailed population and transportation databases. For instance, the recently developed GLobal Epidemic and Mobility (GLEaM) model [70] integrates census and mobility data in a fully stochastic meta-population model that allows for the detailed simulation of the spread of influenza-like illnesses (ILI) around the globe. Meta-population models are also amenable to the inclusion of an age structure in the population by simply modifying the compartmental structure to include the age group contact matrix, M, taking them one step further in terms of realism while still keeping all the advantages of the conceptual clarity that are the hallmarks of this class of models.

Agent-based models, where each agent represents a simplified human individual going through their daily activities, push to the limits the realism of data-driven models. Infection spreads from individual to individual whenever they come into contact with each other, whether within the household, at school or work, or at random in the general population [14]. A key feature of models such as CommunityFlu [71], Flute [72] and Epifast [73] is the characterization of the network of contacts among individuals based on realistic data-driven models of the socio-demographic structure of the population being considered [74,75]. All these highly structured models provide a novel approach to evidence-based and quantitative scenario analysis. Although even among modelers there are contrasting opinions, those models are assuming increasing relevance in the public health domain, providing rationales and quantitative analysis to support the decision- and policy-making processes.

CONCLUSIONS AND FUTURE CHALLENGES

Although in recent years our understanding of dynamical processes in complex networks has progressed at an exponential pace, there are still a number of major challenges that see the research community actively engaged. The first challenge stems from the fact that the analysis of dynamical processes is generally performed in the presence of a timescale separation between the network evolution and the dynamical process unfolding on its structure. At one extreme we can consider the network as quenched in its connectivity pattern, thus evolving on a timescale that is much longer that the dynamical process itself. At the other extreme, the network is evolving at a much shorter timescale than the dynamical process, thus effectively disappearing from the definition of the interaction among individuals that is conveniently replaced by effective random couplings. While the timescale separation is extremely convenient for the numerical and analytical tractability of the models, networks generally evolve on a timescale that might be comparable to that of the dynamical process. Furthermore, the network properties that inform models generally represent a time-integrated static snapshot of the system. However, in many systems the timing and duration of interactions define processes on a timescale very different from, and often conflicting with, those of the time-integrated view. This makes clear the importance of considering the concurrency of network evolution and dynamical processes in realistic models in order to avoid misleading conclusions [76–79].

A second challenge is the co-evolution of networks with the dynamical process. Access to the mathematical and statistical laws that characterize the interplay and feedback mechanisms between the network evolution and the dynamical processes is extremely important, especially in social systems where the adaptive nature of agents is of paramount importance [58,78,80]. The spreading of an opinion is affected by interactions between individuals, but the presence and/or establishment of interactions between individuals is affected by their opinion. This issue is more and more relevant in the area of modern social networks populating the information technology ecosystem, such as those defined by the Facebook and Twitter applications. In this case the network and the information spreading cannot be defined in isolation, especially because of the rapidly changing interactions and modes of communication that depend upon the type of information exchanged and the rapidly adaptive behavior of individuals (Figure 27.7).

The adaptive behavior of individuals to the dynamical processes they are involved in represents another modeling challenge, as it calls for the understanding of the feedback among different and competing dynamical processes. For instance, relatively little systematic work has been done to provide coupled behavior–disease models able to close the feedback loop between behavioral changes triggered in the population by an individual's perception of the disease spread and the actual disease spread [59,81]. Similar issues arise in many areas where we find competing processes of adaptation and awareness of information or knowledge spreading in a population.

Finally, the eventual goal is not only to understand complex systems, mathematically describe their structure

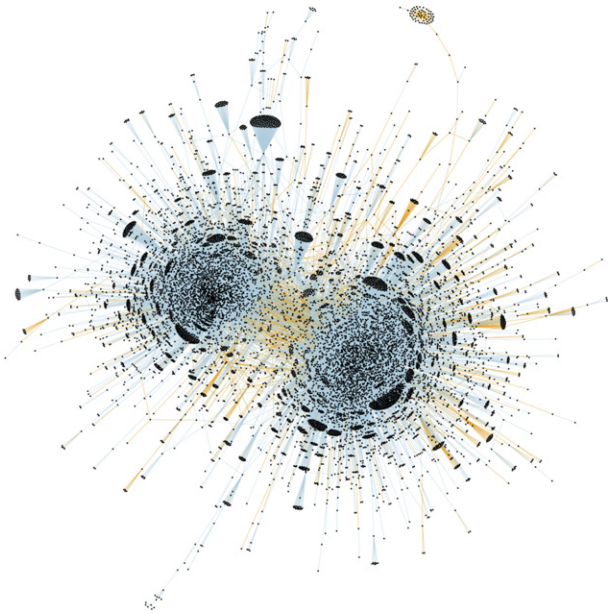


FIGURE 27.7 Each node represents a Twitter user that employed the #bahrain hashtag. Blue and orange edges represent information exchanged between users through the use of retweets and replies, respectively. The two clusters observed correspond to two communities, an English- and an Arabic- speaking one. Retweets are used predominantly to communicate within a single cluster, whereas mentions are employed to send information from one community to the other.

and dynamics, and predict their behavior, but also to control their dynamics. Also in this case, although control theory offers a large set of mathematical tools for steering engineered and natural systems, we have yet to understand how the network heterogeneities influence our ability to control the network dynamics and how network evolution affects controllability [82].

Taking into account the complexity of real systems in epidemic modeling has proved to be unavoidable, and the corresponding approaches have already produced a wealth of interesting results. While this has stimulated the recent focus on large-scale computational approach to epidemic modeling it is clear that many basic theoretical questions are still open. How does the complex nature of the real world affect our predictive capabilities in the realm of computational epidemiology? What are the fundamental limits in epidemic evolution predictability with computational modeling? How do they depend on the level of accuracy of our description and knowledge on the state of the system? Tackling such questions necessitates exploiting several techniques and approaches. Complex systems and networks analysis, mathematical biology, statistics, non-equilibrium statistical physics and computer science all play an important role in the development of a modern computational epidemiology approach. While such an integrated approach might still be in its first steps, it seems now possible to ambitiously imagine the creation of computational epidemic forecast infrastructures able to provide reliable, detailed and quantitatively accurate predictions of global epidemic spread.

REFERENCES

[1] Anderson RM, May RM. Spatial, temporal and genetic heterogeneity in host populations and the design of immunization programs. IMA J Math Appl Med Biol 1984;1:233–66.

[2] May RM, Anderson RM. Spatial heterogeneity and the design of immunization programs. Math Biosci 1984;72:83–111.

[3] Chatterjee S, Durrett R. Contact processes on random graphs with power law degree distributions have critical value 0. Ann Probab 2009;37:2332–56.

[4] Bolker BM, Grenfell BT. Chaos and biological complexity in measles dynamics. Proc R Soc Lond B 1993;251:75–81.

[5] Bolker BM, Grenfell BT. Space persistence and dynamics of measles epidemics. Phil Trans R Soc Lond 1995;348:309–20.

[6] Lloyd AL, May RM. Spatial heterogeneity in epidemic models. J Theor Biol 1996;179:1–11.

[7] Grenfell BT, Bolker BM. Cities and villages: infection hierarchies in a measles meta-population. Ecol Lett 1998;1:63–70.

[8] Keeling MJ, Rohani P. Estimating spatial coupling in epidemiological systems: a mechanistic approach. Ecol Lett 2002;5:20.

[9] Ferguson NM, et al. Planning for smallpox outbreaks. Nature 2003;425:681.

[10] Rvachev LA, Longini JIM. A mathematical model for the global spread of influenza. Math Biosc 1985;75:3.

[11] Keeling MJ, Rohani P. Estimating spatial coupling in epidemiological systems: a mechanistic approach. Ecol Lett 1995;5:20–9.

[12] Hufnagel L, Brockmann D, Geisel T. Forecast and control of epidemics in a globalized world. Proc Natl Acad Sci USA 2004; 101:15124.

[13] Longini JIM, et al. Containing pandemic influenza at the source. Science 2005;309:1083.

[14] Ferguson NM, et al. Strategies for containing an emerging influenza pandemic in Southeast Asia. Nature 2005;437:209.

[15] Colizza V, Barrat A, Barthelemy M, Vespignani A. The role of the airline transportation network in the prediction and predictability of global epidemics. Proc Natl Acad Sci 2006;103:2015.

[16] Keeling MJ, et al. Foot and mouth epidemic: stochastic dispersal in a heterogeneous landscape. Science 2001;294:813–7.

[17] Colizza V, Barrat A, Barthelemy M, Vespignani A. The modeling of global epidemics: stochastic dynamics and predictability. Bull Math Biol 2006;68(8):1893–921.

[18] Eubank S, et al. Modelling disease outbreaks in realistic urban social networks. Nature 2004;429:180.

[19] Keeling MJ, Rohani P. Modeling Infectious Disease in Humans and Animals. Princeton University Press; 2008.

[20] Goffman W, Newill VA. Generalization of epidemic theory: an application to the transmission of ideas. Nature 1964;204:225.

[21] Castellano C, Pastor-Satorras R. Thresholds for epidemic spreading in networks. Phys Rev Lett 2010;105:218701.

[22] Peiris JSM, Yuen KY, Stohr K. The severe acute respiratory syndrome. N Engl J Med 2003;349:2431–41.

[23] Lloyd AL, May RM. How viruses spread among computers and people. Science 2001;292:1316.

[24] Eagle N, Sandy Pentland A. Reality mining: sensing complex social systems. Pers Ubiquitos Comput 2006;10:255–68.

[25] Christakis NA, Fowler JH. Social network sensors for early detection of contagious outbreaks. PLoSOne 2010;6:E12948.
[26] Stehle J, et al. High-resolution measurements of face-to-face contact patterns in a primary school. PLoS One 2011;6:e23176.
[27] Barrat A, Barthelemy M, Pastor-Satorras R, Vespignani A. The architecture of complex weighted networks. Proc Natl Acad Sci U S A 2004;101:3747.
[28] Anderson RM, May RM, editors. Infectious Diseases in Humans: Dynamics and Control. Oxford: Oxford Science Publication; 1992.
[29] Guimera R, Mossa S, Turtschi A, Amaral LAN. The worldwide air transportation network: anomalous centrality, community structure, and cities' global roles. Proc Natl Acad sci USA 2005;102:7794.
[30] Pastor-Satorras R, Vespignani A, editors. Evolution and Structure of the Internet: A Statistical Physics Approach. Cambridge: Cambridge University Press; 2004.
[31] Watts DJ, Strogatz SH. Collective dynamics of 'small-world' networks. Nature 1998;393:440.
[32] Barabási A-L, Albert R. Emergence of scaling in random networks. Science 1999;286:509.
[33] Dorogovtsev S, Mendes JFF. Evolution of Networks: From Biological Nets to the Internet and WWW; 2003.
[34] Hethcote HW, Yorke JA. Gonorrhea transmission dynamics and control. Lecture Note in Biomathematics 56. Berlin: Springer; 1984.
[35] Newman MEJ, editor. Networks. An Introduction. Oxford: Oxford University Press; 2010.
[36] Pastor-Satorras R, Vespignani A. Epidemic spreading in scale-free networks. Phys Rev Lett 2001;86:3200.
[37] Colizza V, Pastor-Satorras R, Vespignani A. Reaction−diffusion processes and metapopulation models in heterogeneous networks. Nat Phys 2007;3:276−82.
[38] Barrat A, Barthélemy M, Vespignani A. Dynamical Processes on Complex Networks. Cambridge Univesity Press; 2008.
[39] Moreno Y, Pastor-Satorras R, Vespignani A. Epidemic outbreaks in complex heterogeneous networks. Eur Phys J B 2002;26:521−9.
[40] Hethcote HW. An immunization model for a heterogeneous population. Theor Pop Biol 1978;14:338−49.
[41] Colizza V, Vespignani A. Epidemic modeling in metapopulation systems with heterogeneous coupling pattern: theory and simulations. J Theor Biol 2008;251:450−67.
[42] Ni S, Weng W. Impact of travel patterns on epidemic dynamics in heterogeneous spatial metapopulation networks. Phys Rev E 2009;79:016111.
[43] Pastor-Satorras R, Vespignani A. Epidemic dynamics in finite size scale-free networks. Phys Rev E 2002;65:035108.
[44] Ben-Zion Y, Cohena Y, Shnerba NM. Modeling epidemics dynamics on heterogenous networks. J Theor Biol 2010; 264:197−204.
[45] Absence of epidemic threshold in scale-free networks with degree correlations. Phys Rev Lett 2003;90:028701.
[46] Barthelemy M, Godreche C, Luck J-M. Fluctuation effects in metapopulation models: percolation and pandemic threshold. J Theor Biol 2010;267:554−64.
[47] Balcan D, Vespignani A. Phase transitions in contagion processes mediated by recurrent mobility patterns. Nat Phys 2011; 7:581−5886.
[48] Belik V, Geisel T, Brockmann D. Natural human mobility patterns and spatial spread of infectious diseases. Phys Rev X 2011;1:011011.
[49] Wang, Y., Chakrabarti, D., Wang, C. & Faloutsos, C. Epidemic spreading in real networks: An eigenvalue viewpoint. In 22nd International symposium on reliable distributed systems (SRDS'03)} IEEE Computer Society, Los Alamitos, CA, USA (2003) p.25−34.
[50] Albert R, Jeong H, Barabási AL. Error and attack tolerance of complex networks. Nature 2000;406:378.
[51] Pastor-Satorras R, Vespignani A. Immunization of complex networks. Phys Rev E 2002;63:036104.
[52] May RM, Lloyd AL. Infection dynamics on scale-free networks. Phys Rev E 2001;64:066112.
[53] Hollingsworth TD, Ferguson NM, Anderson RM. Will travel restrictions control the international spread of pandemic influenza? Nature Med 2006;12:497−9.
[54] Volz E, Meyers LA. Epidemic thresholds in dynamic contact networks. J R Soc Interface 2009;6:233−41.
[55] Barrat A, Barthelemy M, Vespignani A. Dynamical Processes in Complex Networks. Cambridge University Press; 2008.
[56] Cohen R, Havlin S, ben-Avraham D. Efficient immunization strageties for computer networks and populations. Phys Rev Lett 2003;91:247901.
[57] Holme P. Efficient local strategies for vaccination and network attack. Europhys Lett 2004;68:908−14.
[58] Gomez-Gardenes J, Echenique P, Moreno Y. Immunization of real complex communication networks. Eur Phys J B 2006; 49:259−64.
[59] Stauffer D, Barbosa VC. Dissemination strategy for immunizing scale-free networks. Phys Rev E 2006;74:56105.
[60] Amaral LAN, Scala A, Barthelemy M, Stanley HE. Classes of small-world networks. Proc Natl Acad Sci U S A 2005;97:11149.
[61] Watts DJ, Muhamad R, Medina DC, Dodds PS. Multiscale, resurgent epidemics in a hierarchical metapopulation model. Proc Natl Acad Sci 2005;102:11157.
[62] Holme P, Newman MEJ. Nonequilibrium phase transition in the coevolution of networks and opinions. Phys Rev E 2007; 74:056108.
[63] Colizza V, Vespignani A. Invasion threshold in heterogeneous metapopulation networks. Phys Rev Lett 2007;99:148701.
[64] Colizza V, Vespignani A. Epidemic modeling in metapopulation systems with heterogeneous coupling pattern: theory and simulations. e-print cond-mat 2007;0706:3647.
[65] Centola D, Gonzalez-Avella JC, Eguiluz VM, San Miguel M. Homophily, cultural drift, and the co-evolution of cultural groups. J Conflict Resolut 2007;51:905−29.
[66] Funk S, Salathe M, Jansen VAA. Modelling the inuence of human behaviour on the spread of infectious diseases: a review. J R Soc Interface 2010;7:1247−56.
[67] Perra N, Balcan D, Goncalves B, Vespignani A. Towards a characterization of behavior−disease models. PLoS One 2011;6:e23084.
[68] Liu YY, Slotine JJE, Barabasi AL. Controllability of complex Networks. Nature 2011;473:7346.
[69] Cooper BS, Pitman RJ, Edmunds WJ, Gay NJ. Delaying the international spread of pandemic influenza. PLoS Med 2006;3:e12.
[70] Balcan D, et al. Multiscale mobility networks and the spatial spreading of infectious diseases. Proc Natl Acad Sci U S A 2009;106:21484.
[71] Community Flu 1.0, Centers for Disease Control and Prevention (CDC), <http://www.cdc.gov/flu/tools/communityflu>

[72] Chao D, Halloran M, Obenchain V, Longini IJ. FluTE, a publicly available stochastic influenza epidemic simulation model. PLoS Comput Biol 2010;6:e1000656.
[73] Bisset KR, Chen J, Feng X, Kumar VA, Marathe MV. EpiFast: a fast algorithm for large scale realistic epidemic simulations on distributed memory systems. In: Proceedings of the 23rd International Conference on Supercomputing (ICS); 2009 p. 430–439.
[74] Ajelli M, Merler S. The impact of the unstructured contacts component in influenza pandemic modeling. PLoS One 2008;3:e1509.
[75] degli Atti MLC, et al. Mitigation measures for pandemic influenza in Italy: an individual based model considering different scenarios. PLoS One 2008;3:E1790.
[76] Morris M, Kretzschmar M. Concurrent partnerships and the spread of HIV. AIDS 1997;11:641−8.
[77] Moody J. The importance of relationship timing for diffusion: indirect connectivity and STD infection risk. Soc Forces 2002;81:25.
[78] Goldenberg J, Shavitt Y, Shir E, S.Solomon S. Distributive immunization of networks against viruses using the 'honey-pot' architecture. Nat Phys 2005;1:184−8.
[79] Isella L, et al. What's in a crowd? Analysis of face-to-face behavioral networks. J Theor Biol 2011;271:166−80.
[80] Kitsak M, et al. Identification of influential spreaders in complex networks. Nat Phys 2010;6:888−93.
[81] International Air Transport Association, <http: //www.iata.org>
[82] Official Airline Guide, <http: //www.oag.com>