CHAPTER 3

DATA MODEL INTEGRATION: THE GLOBAL EPIDEMIC AND MOBILITY FRAMEWORK

GIVEN A SET OF INITIAL CONDITIONS for the local outbreak of a new potentially pandemic pathogen, the timeline of the arrival of the epidemic in each country is mainly determined by the human mobility network that couples different regions of the world. By looking at individual countries or a given continent in isolation, any estimate of the epidemic timeline would be based on assumptions about imported cases from the rest of the world. Human mobility patterns are hence key to consistently simulating the mobility of infectious individuals on the global scale, and thus providing ab initio estimates of the epidemic timeline in each country or urban area without assumptions on case importation.

The Global Epidemic and Mobility (GLEAM) framework produces realistic simulations of the global spread of infectious diseases with this in mind. It integrates (**FIGURE 3.1**) three data layers:

Figure 3.1 | GLEAM data layers

The three data layers integrated into the GLEAM computational modeling framework.

- An individual-based stochastic mathematical model of the infection dynamics
- Real-world data on the mobility of this population
- Real-world data on the global population

The real-world population and mobility data discussed in the previous chapter are used to determine when and where people will interact and potentially transmit the infection. In order to do that, GLEAM divides the world into a grid of small square cells. Satellite and census sources are used to calculate the population density in each of these cells, which are then clustered into subpopulations centered on their nearest transportation hub.

HUMAN MOBILITY PATTERNS ARE THE KEY TO CONSISTENTLY SIMULATING THE MOBILITY OF INFECTIOUS INDIVIDUALS ON THE GLOBAL SCALE.

GLEAM simulates human mobility and disease spreading in a sequence of time steps (representing full days). Within each population cluster, the spread of the infection among individuals is governed by the characteristics of the disease and the containment and mitigation responses specified in the epidemic model. The disease is transmitted between population clusters when people commute to work or school or travel longer distances on national and international flights. On high-performance computers, GLEAM executes millions of stochastic simulations, making it possible to generate for each population the statistical ensemble of possible epidemic evolutions and analytics for quantities such as newly generated cases, seeding events, time of arrival of the infection, and others.

BUILDING A SYNTHETIC WORLD

The GLEAM framework is based on a metapopulation approach in which the world is divided into geographical regions defining a subpopulation network where connections among subpopulations represent the individual fluxes due to the transportation and mobility infrastructure. The population layer is based on highly detailed data, with a granularity defined by a lattice of cells covering

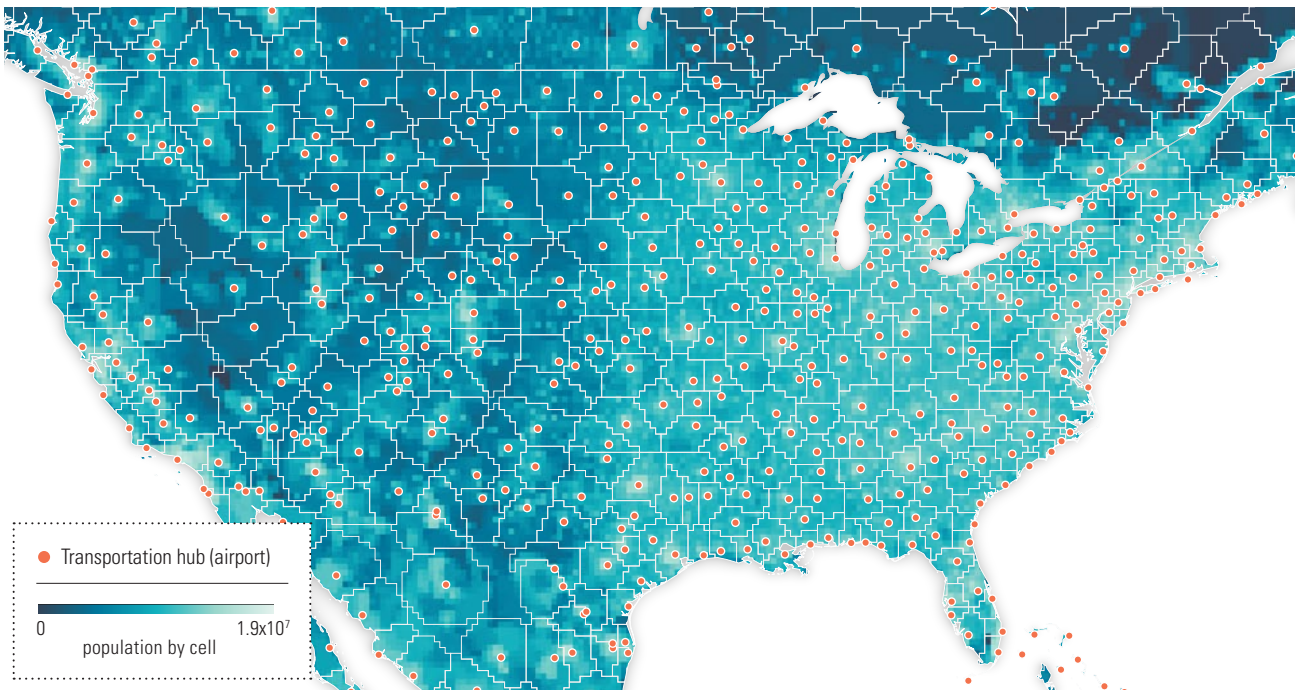
the whole planet at a resolution of 15 x 15 arc minutes (approximately 25 x 25 kilometers). In order to define the subpopulations that constitute the metapopulation structure of the model, a Voronoi tessellation of the Earth's surface is performed, defining census areas centered around the major transportation hubs obtained from the International Air Transport Association (IATA) and OAG database, as shown in **FIGURE 3.2**. By considering the distance between the cells and the transportation hubs, we assign each cell to a specific hub; this process generates over 3,200 subpopulations worldwide or more precisely census areas. In this tessellation, hubs generally correspond to major urban areas and airports. The cells belonging to a subpopulation allow us to determine the population of that census area. Other attributes, such as the age structure of the population, health infrastructures, etc., can be added according to available data.

MOVING PEOPLE AROUND

The spatio temporal patterns of the disease spreading are associated with the mobility flows that couple different subpopulations. These flows constitute the mobility data layer that is represented as a network of connections among subpopulations. This identifies the number of individuals going from one subpopulation to the others. The mobility network is made by different kinds of mobility processes, from short-range commuting to intercontinental flights with time scale and traffic volumes that span several orders of magnitude. The airline system layer integrates air travel mobility, containing the list of worldwide origin-destination flows between airport pairs on a daily schedule.

Figure 3.2 | GLEAM's tessellation of North America

The polygons define the census areas considered by the model. The circles represent the major transportation hub centers of each area. The colors of the census areas are proportional to the population of each cell.



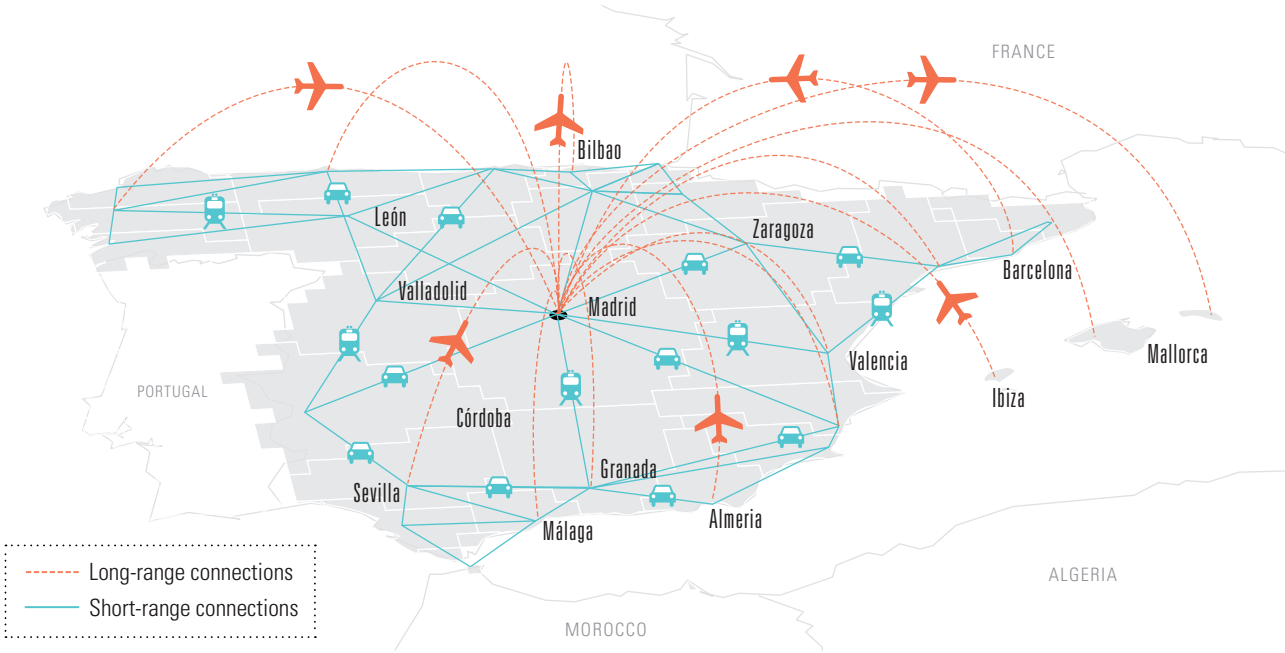


Figure 3.3 | Long- and short-range mobility implementation in GLEAM

Highlighting some of the air transportation connections (orange) and the short-range mobility network (blue) for Madrid, Spain.

Individuals travel on airplanes according to an explicit dynamic that considers the probability for each individual in the population to travel on a specific route.

For the short-range mobility, we rely on databases collected from the Offices of Statistics of 30 countries in five continents. The full dataset includes more than 80,000 administrative regions and over five million commuting flow connections between them. In order to overcome the differences in the spatial resolution of the commuting data across different countries, we define a worldwide homogeneous standard for GLEAM. We use the geographical census areas obtained from the Voronoi tessellation as the elementary units to define the centers of gravity for the process of commuting. This allows us to deal with similar units across the world with respect to mobility which emerge from the tessellation, and not country specific administrative boundaries. We map the different levels of commuting data into the geographical census areas. The mapped commuting flows can be seen as a second transportation network connecting subpopulations that are geographically close. Where data are not available, the short-range mobility layer can be generated synthetically by relying on the so-called gravity law[1,2] and the more recent approach dubbed the radiation law, both calibrated on the real data available.[3] The short-range mobility network can be overlaid on the airline system layer forming the mobility system of the GLEAM synthetic world (**FIGURE 3.3**).[4]

1 Duygu Balcan et al., "Multiscale mobility networks and the spatial spreading of infectious diseases," Proceedings of the National Academy of Sciences **106**, 21484–21489 (2009).
2 Cécile Viboud et al., "Synchrony, waves, and spatial hierarchies in the spread of influenza," Science **312**, 447–451 (2006).
3 Filippo Simini et al., "A universal model for mobility and migration patterns," Nature **484**, 96–100 (2012).
4 Duygu Balcan et al., "Modeling the spatial spread of infectious diseases: The global epidemic and mobility computational model," Journal of Computational Science **1**, 132–145 (2010).

The short-range commuting mobility of individuals is simulated by an effective approach that defines mixing subpopulations and which identifies the number of individuals $N_{ij}(t)$ of the subpopulation i effectively present in subpopulation j at time t (see **INFOBOX 3.1**). This methodology assumes the subpopulation i as having an effective number of individuals $N_{ij} \ll N_{ii}$ in contact with the individuals of the neighboring subpopulation j in a quasi-stationary

3.1 INFOBOX MIXING SUB POPULATIONS

In the case of commuting flows, we assume that individuals in the subpopulation i will visit anyone of the connected subpopulations with a per capita diffusion rate σ_i. As we aim at modeling commuting processes in which individuals have a memory of their location of origin, displaced individuals return to their original subpopulation with rate τ.

In order to model the commuting flows in the subpopulation network, we define mixing subpopulations. At any moment in time, each member of subpopulation i is either in their subpopulation of residence or outside and visiting one of the neighboring subpopulations j. By using the approach developed in Sattenspiel and Dietz (1995)[1] and Keeling and Rohani (2002)[2], we may group the members of i according to the location in which they are actually present at a given time t, $N_{ii}(t)$ and $N_{ij}(t)$ with $j \epsilon v(i)$ where $v(i)$ are the subpopulations connected to i (**FIGURE 3.1.1**). The rate equations for the population sizes of different subgroups can be readily written by explicitly taking into account the mobility rates along the edges of the subpopulation network. This system of rate equations has a characteristic relaxation time that can be obtained by solving the appropriate differential equations. In particular, it is possible to show under the general assumption of $\sigma_i << \tau_i$ that the relaxation characteristic time is τ_i^{-1} and that the mixing subpopulations read as:

$$N_{ii} = \frac{N_i}{1+\sigma_i/\tau_i} \text{ and } N_{ij} = \frac{N_i}{1+\sigma_i/\tau_i}\,\sigma_{ij}/\tau_i$$

This implies that in the regime $\sigma_i << \tau_i$, $N_i(t)$ represent a small perturbation to the overall subpopulation of size N_j. These expressions are used to obtain the effective force of infection taking into account the interactions generated by the commuting flows.

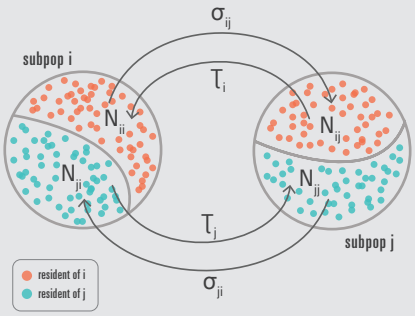


Figure 3.1.1 | Illustration of commuting and subdivision of population

At any time each subpopulation is occupied by its residents plus visitors from its neighbors. For instance, the population in subpopulation i is divided between individuals who reside and are present in the subpopulation (N_{ii}) and those who are residents in subpopulation j but present in subpopulation i (N_{ji}). Different classes of people move between connected subpopulations along the edges at the rates shown.

Adapted from D. Balcan and A. Vespignani, "Invasion threshold in structured populations with recurrent mobility patterns." J. Theor. Biol 293 (2012)

1 L. Sattenspiel and K. Dietz, "A structured epidemic model incorporating geographic mobility among regions," Mathematical Biosciences 128, 71–91 (1995).

2 Matt J Keeling and Pejman Rohani, "Estimating spatial coupling in epidemiological systems: a mechanistic approach," Ecology Letters 5, 20–29 (2002).

state, reached whenever the time scale of the epidemic spreading is larger than the commuting rate.

THE DISEASE DYNAMIC

Superimposed on the worldwide population and mobility layers is the epidemic model that defines the disease and population dynamics. Individuals move around and transmit the infection via the interactions with other people. The infection dynamics takes place within each subpopulation and assumes the classic compartmentalization scheme for the characterization of the disease (**FIGURE 3.4**). Each individual fits, at any given point in time, within a certain compartment that corresponds to a particular disease-related state (being, e.g., susceptible, symptomatic, or vaccinated). These compartments are connected by transitions that define how individuals may pass from one state to another (e.g., from susceptible to latent when being infected), while the associated parameters determine the likelihood that such transitions take place. GLEAM uses algorithms mathematically defined through individual-based stochastic processes to calculate the proportion of the population within each compartment for each subpopulation and how these proportions change

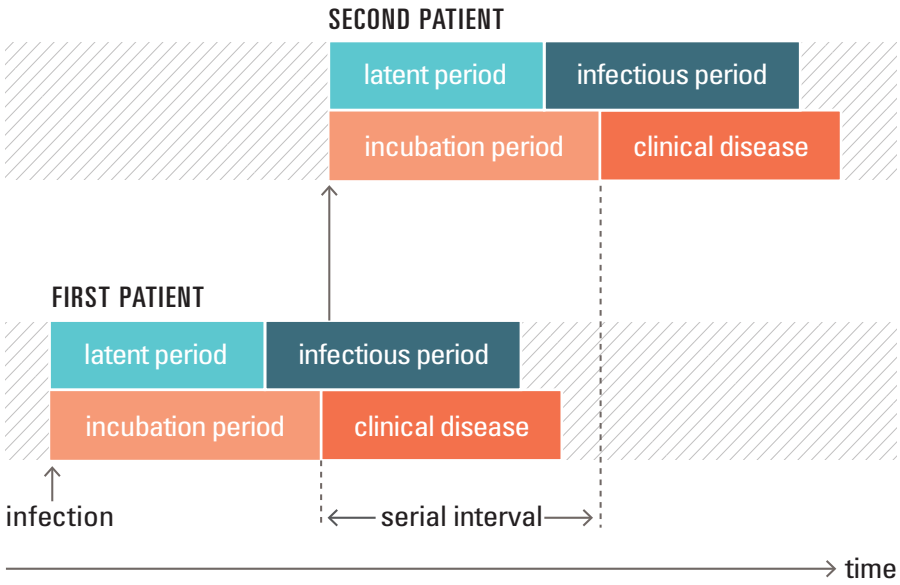


Figure 3.4 | Summary of basic definitions of the stages of a disease

As a function of time, the disease's evolution in two patients. Individuals who have not been in contact with the pathogen are generally labeled as susceptible. The pre infectious period, also called the latent period, defines the time from infection to when the host is on her turn able to transmit the infection. The incubation period is the time from infection to the onset of clinical symptoms. The infectious period is the time period in which the host can transmit the infection to other hosts. The clinical disease time refers to the duration of the clinical symptoms. It is important to stress that the time of each period can change in the case of pharmaceutical interventions specific to the disease considered. Some diseases may also require more detailed classification of the states characterizing the natural history of the disease.

over time as individuals transition from one compartment to the next (**INFOBOX 3.2**). The progression of the disease is then simulated at the individual level. GLEAM can also include the age structure of individuals in defining the transitions. It is clear that no model fits all diseases, and GLEAM needs the detailed process describing the evolution of the illness within each individual and the transmission process. In general, this is specified by the so-called natural history of the disease that maps the time-periods of the disease

3.2 INFOBOX MODELING THE DISEASE TRANSMISSION

Although the realistic modeling of infectious diseases generally implements much more complicated compartmental structures, let's use as an example the basic compartmental structure where individuals can only ever be in one of three states: susceptible, infectious, and recovered. This simple three-state compartmentalization defines the classic susceptible-infected-recovered (SIR) model. In this case we have only two possible transitions. The first, denoted $S \rightarrow I$, is when a susceptible individual interacts with an infectious one and becomes infected. The second one, denoted $I \rightarrow R$, occurs when the infectious individual recovers from the disease and is assumed to have acquired permanent immunity from the disease. The two processes completely determine the epidemic evolution. The $I \rightarrow R$ transition is spontaneous and occurs after the individual has spent a certain time fighting the disease or taking a specific medical treatment; in other words the transition does not depend on any interaction with the other individuals in the population. The $S \rightarrow I$ transition instead occurs only because of the contact/interaction of the susceptible individual with an infectious individual. In this case the interaction dynamics between people is a specific feature of the transition and has to be taken into account. The conceptual abstraction of the SIR compartmental model is well represented by the flow diagram of **FIGURE 3.2.1** in which the different compartment transitions are schematized through arrows that indicate the possible change of state of the individuals.

The $I \rightarrow R$ transition is obviously the simplest one to model. For many type of diseases, the amount of time spent in the infectious class is distributed around a well-defined mean value. For the sake of realism, the probability that one person will move from the I class to the R class depends on how much time he/she has spent in the I class. The distribution of the "infectious period" and the transition probability can generally be estimated from clinical data; however, from a simplistic modeling assumption, the probability of transition is assumed constant. In this way it is possible to define a transition probability per unitary timestep μ, called the recovery probability. Since we are dealing with a probability per unit time, the time an individual will spend on average in the infectious compartment, the mean infectious period, is equal to μ^{-1}.

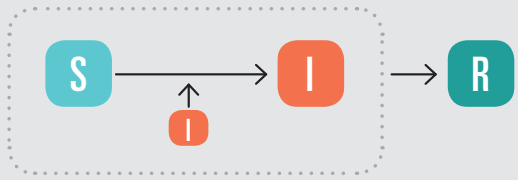


Figure 3.2.1 | Flow diagram of the SIR model

The model allows only the $S \rightarrow I$ and the $I \rightarrow R$ transitions. The transitions are denoted by arrows going from one compartment to the other. The $S \rightarrow I$ transition occurs only in the presence of a contact/interaction with infectious individuals. For this reason the transition arrow has a line callout to the infectious compartment.

The definition of the transition probability in the case of the $S \rightarrow I$ transitions is more complicated than the recovery transition. The probability that a susceptible individual moves into the infectious compartment depends on the number of contacts with infectious people and the probability that in each contact with an infectious individual the disease is transmitted to the susceptible. The number of contacts with infectious individuals depends in turn on the per capita number of contacts per unit time with other individuals and the total number of infectious people present in the population. In the GLEAM framework, the transmission dynamics can be simulated at different levels of detail (see **FIGURE 3.2.2**). ▸

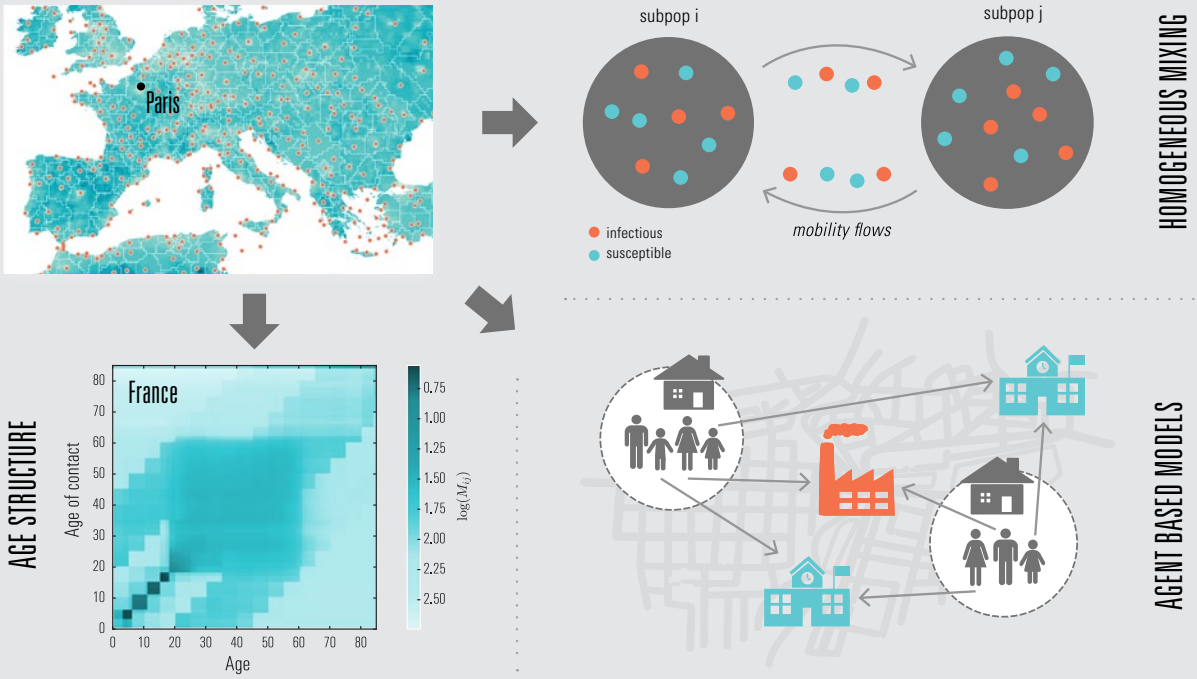


Figure 3.2.2 | Multiple schemes for the stochastic intra-population contagion dynamic

The simplest approaches consider chain binomial processes in which the discrete individuals are indistinguishable and characterized only by their compartmental state. These models can be made more realistic by including age structure or other features of the individuals. In this case the transmission of the disease is described by parameters that depend on those features. An example is provided by models implementing specific contact matrices that characterize the number of contacts among individuals in different age brackets.

At the finer level, synthetic population constructions are even more refined and consider a classification of location such as households, schools, offices, etc. The movements and time spent in each location can be used to generate individual-location bipartite networks whose unipartite projection defines the individual level, synthetic interaction network that governs the epidemic spreading. Also in this case, although the model underlying the computational approach is a network model, each individual is annotated with the residence place, age, as well as many other possible demographic information that can be exploited in the analysis of the epidemic outbreak. Detailed synthetic populations thus reconstruct a statistically equivalent picture of the actual population down to the level of the granularity of the data available.

For the sake of simplicity, let us consider here the example of a homogenous mixing approximation which assumes that individuals randomly interact among them. According to this minimal framework, the larger the number of sick and infectious people among one individual's contacts, the higher the probability of infection transmission. This readily translates in the definition of the force of infection λ, also called risk, that expresses the probability per unit time at which susceptible individuals may contract the infection. In the limit of small risk, it is possible to derive the explicit form $\lambda = \beta I_t / N$. Here β defines the transmissibility, average number of transmissions per unit time, that depends on the specific disease as well as the contact pattern of the population,

I_t the total number of infectious individuals at time t; I_t/N is therefore the density of infected individuals in the population. This form of the force of infection is called the *mass action law* and is used in many other reaction-diffusion problems in chemistry and physics. It is important to note that the force of infection is said to be *frequency dependent* as it assumes that the number of contacts is independent of the population size. Therefore, the force of infection depends only on the density of infectious individuals, and decreases for larger populations all the other factors being equal. This is indeed an assumption that fits with our intuition as the probability of getting infected by one single infectious individual in a city like Paris with about two million residents is necessarily much lower than the probability to be infected by the same infectious individual in Bloomington, Indiana, a campus town with only 80,000 residents.

In order to translate the above formal relation into an explicit equation, we can define the variables S_t, I_t and R_t denoting the number of individuals in the susceptible, infectious, and recovered compartment at time t, respectively. Given the assumption that μ and β are constant, we can easily define the associated stochastic processes that relate the stochastic variables at time t with the variables at time $t+1$ in the form of a simple binomial model of transmission for discrete contacts and discrete time. Each susceptible individual has a probability $\lambda_t = \beta I_t/N$ to contract the disease and transit to the infectious state.

As we assume to have S_t independent events occurring with the same probability, the number of new infected individuals I_+ generated at time $t+1$ is a random variable that will follow the binomial distribution $I_+ \sim Bin(S_t, \lambda_t)$. The binomial distribution provides the probability that among the S_t independent trials with probability λ_t, we have y positive events at time $t+1$. Analogously, the number of new recovered individuals at time $t+1$ is a random variable that will follow a binomial distribution $R_+ \sim Bin(I_t, \mu)$, where the number of independent trials is given by the number of infectious individuals I_t that might recover and the probability of recovery in a timestep is given by the recovery probability μ. If we consider a specific value of the stochastic variables S_t, I_t and R_t, the stochastic equations regulating the behavior of the epidemic can be written as:

$$s_{t+1} = s_t - Bin(s_t, \lambda_t)$$
$$i_{t+1} = i_t + Bin(s_t, \lambda_t) - Bin(i_t, \mu)$$
$$r_{t+1} = r_t + Bin(i_t, \mu),$$

where $Bin(s_t, \lambda_t)$ and $Bin(i_t, \mu)$ are two random variables distributed according to the respective binomial distribution. It is worth remarking here that the unitary time step defines an actual time scale Δt and that the transition probability must be defined as a function of this time scale.

In the SIR model it is possible to readily calculate the basic reproduction number explicitly as $R_0 = \beta/\mu$. It is given simply by the transmissibility times the average duration of the infectiousness of the single individual; this provides the average secondary infections per infectious individual.

In such a computational approach, we deal with stochastic systems, and therefore we need to generate random variables according to the specified probability distributions defined in the model. In a stochastic simulation, each sequence of random values is generated through a random number generator. Each different random input therefore provides a single stochastic instance of the system's behavior. In the case of epidemic models, each stochastic realization will represent only one of the many possible epidemic outcomes that the same model with the same initial conditions and parameters can generate. A careful analysis of the quality of the random number generator used is advisable in all intensive large-scale computational applications.

The simple example discussed here has to be generalized to the more complicated compartmental structures used by GLEAM for the realistic modeling of infectious diseases. In many cases this implies the use of more advanced mathematical constructions and the use of multinomial stochastic processes.

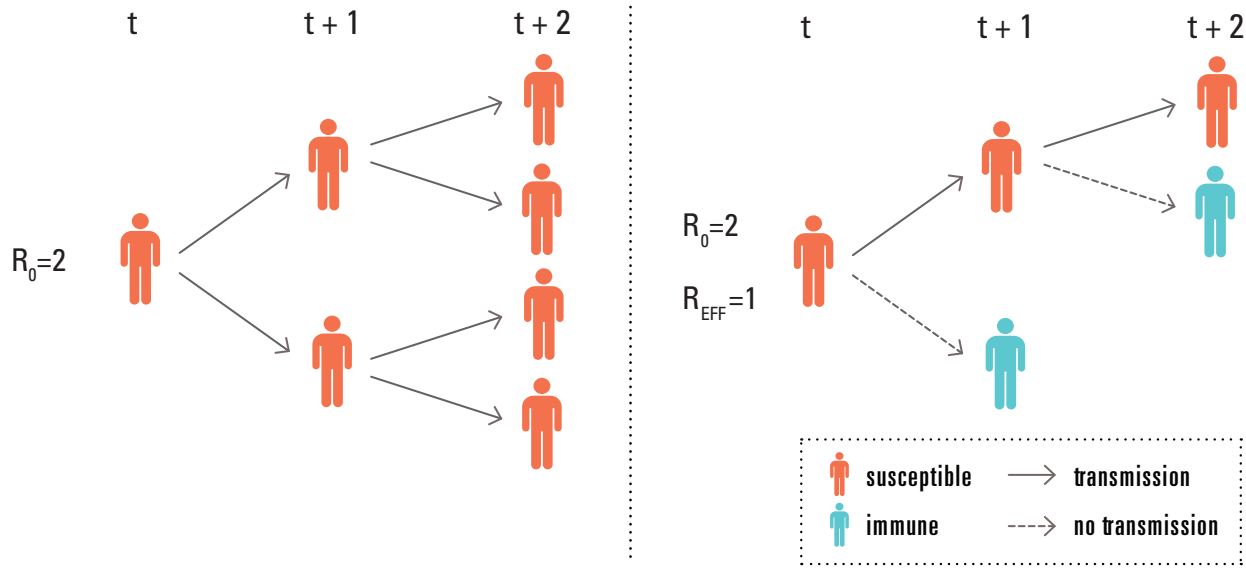


Figure 3.5 | Illustration of the chain of transmissions as a branching process

Each infectious individual generates a number of secondary cases according to the model transmission rate and the available susceptible individuals. The branching ratio of this process, defined as the average number of secondary generations in a fully susceptible population, defines the basic reproduction number or ratio, R_0. One of the main targets of public health intervention is the reduction of the transmissibility, for instance, by vaccinating a fraction of individuals, resulting in an effective reproduction number R_{eff} smaller than one.

progression. In **INFOBOX 3.3**, we show the basic compartmental structure of some of the diseases we will consider. It is important to note that it is possible to define more compartmental states by also considering the implementation of pharmaceutical and non-pharmaceutical interventions such as hospitalization, vaccination, quarantine, isolation, and so on. In addition, in GLEAM it is important to associate with each compartment the likelihood that the individual will travel long distance, commute, etc. In many cases, clinical symptoms are associated with reduced or no mobility of the sick individual. This is also true for compartments signaling the isolation or quarantine of individuals. Each compartment, therefore, carries additional information of the mobility and the potential interaction of the individual.

The disease progression is mostly defined by two quantities generally used to quantify the transmissibility potential and spreading time scale of the disease. The first quantity is the *basic reproduction number, R_0*, that is the average number of secondary cases produced by a primary case in a fully susceptible population. If each infectious individual does not generate a number of infectious individuals larger or equal to one, the number of infectious individuals will generally decrease, and the transmission chain will die out before an epidemic can take place. However, if each infectious individual generates more than one infectious individual in the transmission process, the number of infectious individuals will continue to increase in time. Intuitively, the larger the R_0, the more transmissible the disease is and the faster the number of cases will grow (**FIGURE 3.5**). Together with the basic reproduction number, the generation time G_t of the disease, defined as the time occurring from the infection of the host to the end of the infectious period, is also an important quantity that defines the time scale of the disease. For the same R_0, a smaller generation time indicates a much faster progression of the disease, as the

Disease Type	R_0 Value
SARS	2 – 3
HIV	2 – 5
Smallpox	5 – 10
Pandemic Influenza	1.5 – 3.5
Ebola	1.5 – 3.5

Table 3.1 | Reproduction number

Ranges for the reproduction number of some infectious diseases.

same number of secondary cases are generated in a shorter time window. In general, a measure of the generation time is clinically offered by the *serial interval*: the time from the onset of a primary case to the onset of the secondary case. R_0 is a function of the parameters describing the natural history of the disease and can be calculated explicitly in different models (**INFOBOX 3.2**). Often, the level of threat of an infectious disease is measured as a function of the R_0.

THE BASIC REPRODUCTION NUMBER, R_0, IS THE AVERAGE NUMBER OF SECONDARY CASES PRODUCED BY A PRIMARY CASE IN A FULLY SUSCEPTIBLE POPULATION.

SYNTHETIC EPIDEMICS

GLEAM defines a synthetic world in which we can simulate with the computer the unfolding of epidemics and pandemics. Each simulated time step represents a full day. The model needs the definition of the initial conditions that specify the number and location of individuals capable of transmitting the disease. At the start of the time step, we use the flight network to move travelers to their destination.

As a consequence, the arrival time for the infection is the day at which the first infected traveler arrives, and this seed individual is considered to have the chance of infecting others. The probability of traveling changes from day to day and can be generalized in order to consider the effects of location specific

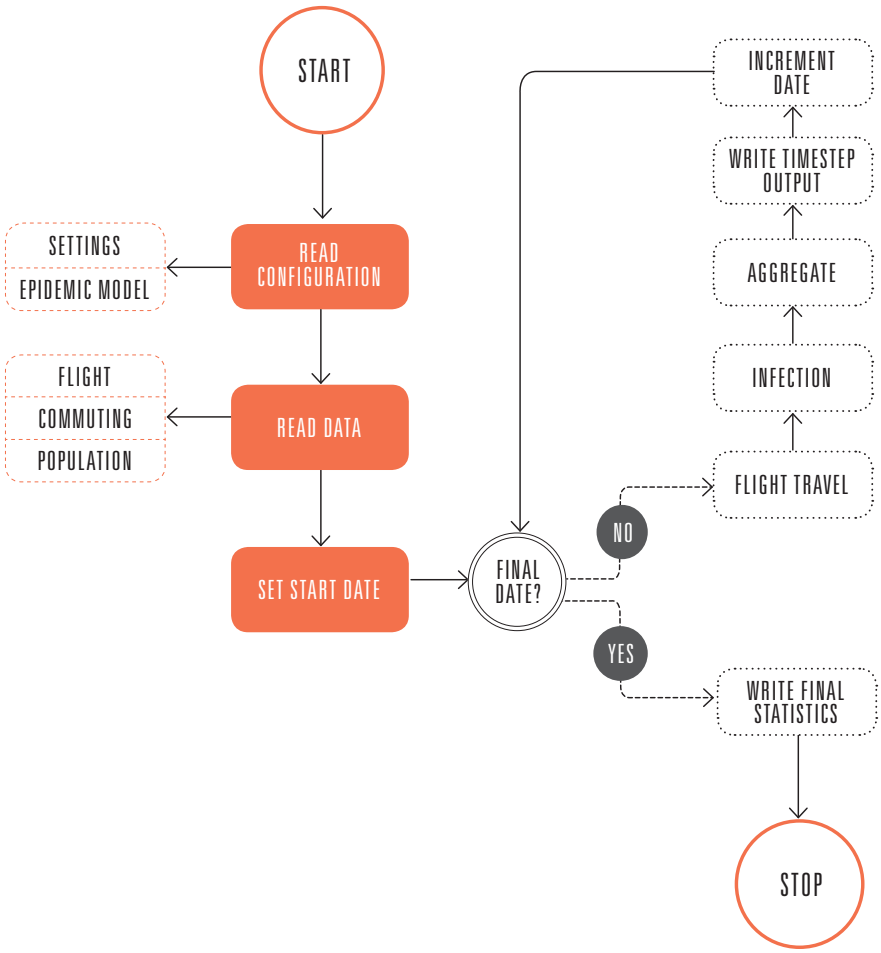


Figure 3.6 | GLEAM engine flow chart

The full procedure used by the GLEAM simulation engine. The left column represents input databases. The program flow occurs along the center.

3.3 INFOBOX DISEASE COMPARTMENTAL STRUCTURE

GLEAM labels individuals in each population according to the compartment describing the state of the disease and the possibility to travel, commute, etc.

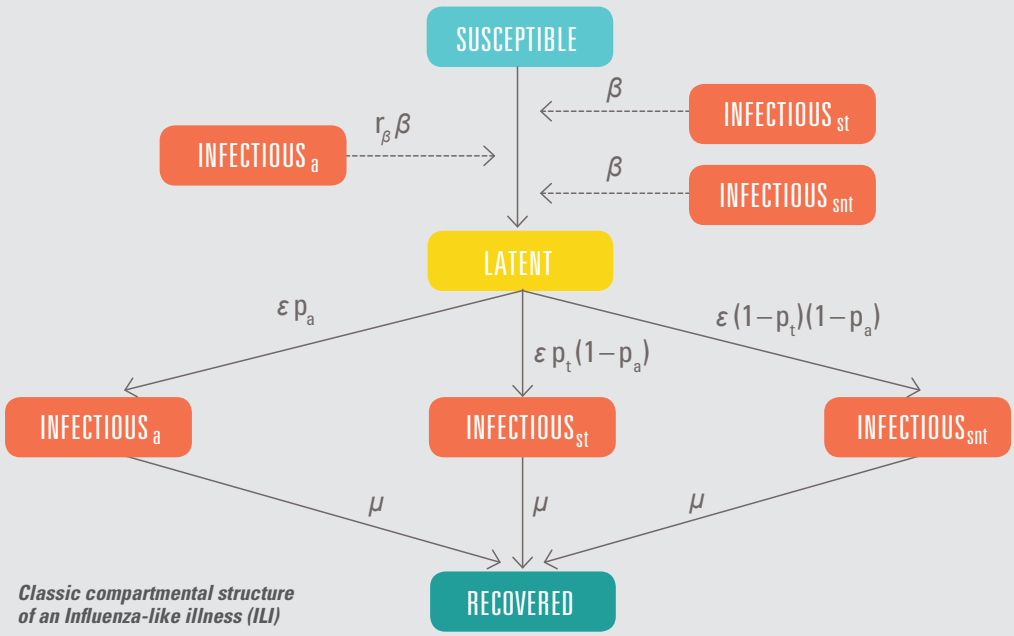
Influenza

A susceptible individual in contact with a symptomatic or asymptomatic infectious person contracts the infection at rate β or $r_\beta \beta$, respectively, and enters the latent compartment where he is infected but not yet infectious.

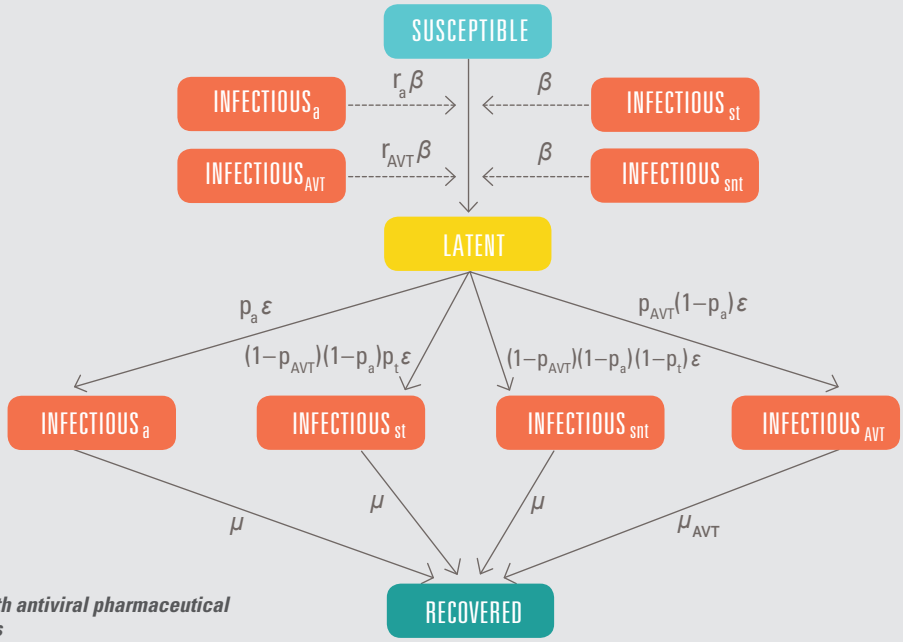
At the end of the latency period ε^{-1}, each latent individual becomes infectious, entering the symptomatic compartments with probability $1–p_a$ or becoming asymptomatic with probability p_a. The symptomatic cases are further divided between those who are allowed to travel (with probability p_t) and those who would stop traveling when ill (with probability $1–p_t$). Infectious individuals recover permanently with rate μ.

Influenza with antiviral pharmaceutical interventions

A modified Susceptible-Latent-Infectious-Recovered model is considered to take into account the use of antiviral drugs as a pharmaceutical measure. In particular, infectious individuals are subdivided into: asymptomatic (Infectious_a), symptomatic individuals who travel while ill (Infectious_{st}), symptomatic individuals who restrict themselves from travel while ill (Infectious_{snt}), and symptomatic individuals who undergo the antiviral treatment (Infectious_{AVT}). A susceptible individual interacting with an infectious person may contract the illness with rate β and enter the latent compartment where he/she is infected but not yet infectious. The infection rate is rescaled by a factor r_a in case of asymptomatic infection and by a factor r_{AVT} in case of a treated infection. At the end of the latency period, of average duration equal to ε^{-1}, each latent individual becomes infectious, showing symptoms with probability $1–p_a$, and asymptomatic with



Classic compartmental structure of an Influenza-like illness (ILI)



Influenza with antiviral pharmaceutical interventions

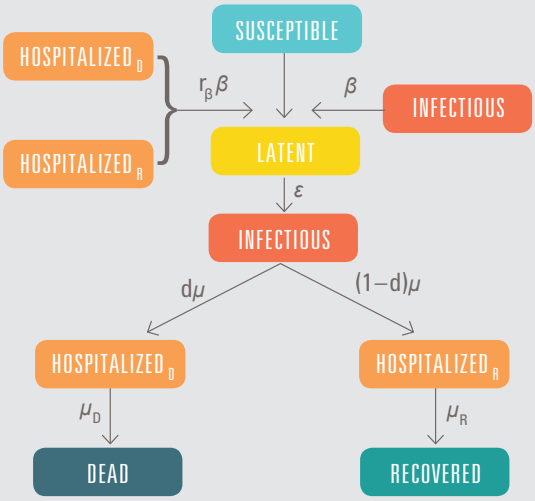
probability p_a. Change in traveling behavior after the onset of symptoms is modeled by p_t, which is the probability that individuals would continue traveling when ill. Infectious individuals recover permanently after an average infectious period μ^{-1}. We assume the antiviral treatment regimen is administered with p_{AVT} to the symptomatic infectious individuals within 1 day from the onset of symptoms, reducing the infectiousness and shortening the infectious period by one day.

SARS-like viruses and their non-pharmaceutical containment

The population of each city is classified into seven different compartments, namely, susceptible, latent, infectious, hospitalized who either recover or die, dead, and recovered individuals. We assume that hospitalized, as well as infectious individuals are able to transmit the infection, given the large percentage of the cases that were seen among healthcare workers. The actual efficiency of hospital isolation procedures is modeled through a reduction of the transmission rate β by a factor r_β = 20%, as estimated for the early stage of the epidemic in Hong Kong. The infectiousness of patients in the hospitalized compartments HR and HD are assumed to be equal (although this assumption can easily be changed in the model). Susceptible individuals exposed to SARS enter the latent class. Latents represent infected individuals who are not yet contagious and are assumed to be asymptomatic, as suggested by results based on epidemiological, clinical, and diagnostic data in Canada. They become infectious after an average time ε^{-1} (mean latency period). Individuals are classified as infectious during an average time equal to μ^{-1}, from the onset of clinical symptoms to their admission to the hospital where they eventually die or recover. Patients admitted to the hospital are not allowed to travel. The average periods spent in the hospital from admission to death or recovery are equal to μ_D^{-1} and μ_R^{-1}, respectively. The average death rate is denoted by d.

Viral hemorrhagic fever compartmental model

Legrand et al.[1] introduced a compartmental model for VHF virus where the individuals are classified in the following way: susceptible individuals S, who can acquire the disease after contact with infectious individuals, latent individuals L who are infected but do not transmit the disease and are asymptomatic, infectious ▸

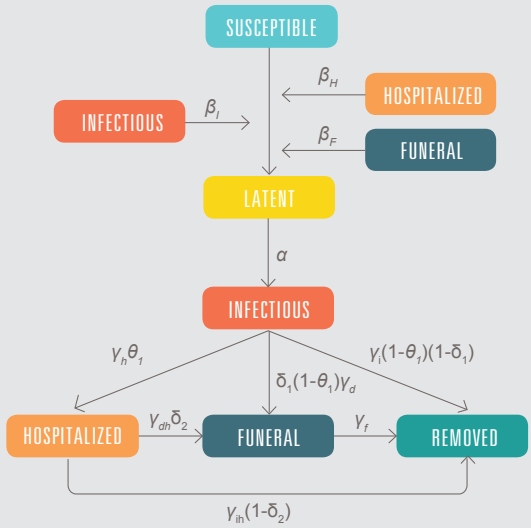


SARS-Like viruses and their non-pharmaceutical containment

individuals I who can transmit the disease and are symptomatic, hospitalized infectious individuals H, dead individuals F that can infect through the burial ceremonies, and removed individuals R. The most distinctive feature of this model is that dead individuals can still transmit the disease.

Susceptible individuals, after contact with an infectious individual (I, H or F), enter the latent class at a rate β_I, β_H, or β_F. At the end of the latency period α^{-1}, each individual becomes infectious. Infectious individuals then can transition to the hospitalized, funeral, or removed compartments according to different parameters. Similarly, from the compartment hospitalized and funeral, individuals can enter the removed compartment. The mean duration from onset of symptoms to hospitalization is γ_h^{-1}, γ_{dh}^{-1} is the mean duration from hospitalization to death, and γ_i^{-1} denotes the mean duration of the infectious period for survivors. The mean duration from hospitalization to end of infectiousness for survivors is γ_{ih}^{-1}, and γ_f^{-1} is the mean duration from death to burial.

θ_1 is computed so that θ% of infectious cases are hospitalized. δ_1 and δ_2 are defined such that the overall case-fatality ratio is δ.



Viral hemorrhagic fever compartmental model

1 Judith Legrand, Rebecca Freeman Grais, Pierre-Yves Boëlle, Alain-Jacques Valleron, and Antoine Flahault, "Understanding the dynamics of ebola epidemics," Epidemiology & Infection 135, 610–621 (2007).

airline traffic reductions. The short-range mobility and the infection dynamics are modeled together by defining the probability of transition and risk of infection acting on each individual in each subpopulation. This process is repeated for every simulated day, keeping track of all the individuals and their traveling patterns as shown in the pseudo-code for the GLEAM algorithm (**FIGURE 3.6**).

GLEAM also allows the introduction of seasonal variations in the transmissibility of the disease, such as in the case of influenza. Seasonality effects are still an open problem in the transmission of ILI. In order to include the effect

of seasonality on the observed patterns of ILI, a standard empirical approach can be used in which seasonality is modeled by a forcing that reduces the basic reproduction number by a factor ranging from 0.1 to 1 (no reduction). This forcing is described by a sinusoidal function over a 12-month period that reaches its peak during winter time and its minimum during summer time in each hemisphere, with the two hemispheres at opposite phases. The minimum rescaling of α_{min} of the reproduction number is a free parameter to be estimated from data. For scenario purposes it is possible to consider a mild seasonality and a strong seasonality scenario, with α_{min} ~0.5 and α_{min} ~0.1, respectively.[5]

Given the population and mobility data, infection dynamics parameters, and initial conditions, GLEAM performs the simulation of stochastic realizations of the worldwide unfolding of the epidemic. From these in silico epidemics, a variety of information can be gathered, such as the prevalence, morbidity, number of secondary cases, number of imported cases, hospitalized patients, amounts of drugs used, and other quantities for each subpopulation with a time resolution of 1 day. In the next chapter, we will see the results of the numerical simulations and why and how they can be useful to our analysis and understanding of infectious disease spreading.

IF EACH INFECTIOUS INDIVIDUAL GENERATES MORE THAN ONE INFECTIOUS INDIVIDUAL, THE NUMBER OF INFECTIOUS INDIVIDUALS WILL INCREASE IN TIME.

5 Ben S. Cooper et al., "Delaying the International Spread of Pandemic Influenza," PLoS Med **3**, e212 (2006).