

1 Network Epidemiology

Epidemiology is the study of diseases, in all ways and in all aspects. Network epidemiology generally focuses on infectious diseases, meaning diseases that can spread from one person to another. This usually excludes diseases like heart disease or cancer, and focuses instead on transmissible diseases like influenza, coronavirus, dengue, malaria, etc.

The details of infectious diseases can be enormously complicated, and span all scales in biology, from molecular to populations, and even across species. Do we consider the molecular mechanisms of infection, e.g., how a virus gets into a cell? Do we consider what happens to individual cells, e.g., how a virus hijacks a cell's machinery to reproduce, or how bacteria behave in the body? Do we account for how the immune system responds? These are all important questions, but most network-based epidemiological models focus on population dynamics, i.e., how many people are sick, how many could get sick, and how many have recovered.

The combination of population-level dynamics and a network representing people and their interactions is called **network epidemiology**, in which the shape of the network—who connects to whom— influences the spread of the disease. To begin, we'll study a simple model of an epidemic without network structure, in order to develop intuition about its dynamics before adapting that model to run over a network.

1.1 The simplest epidemic : the compartmental model

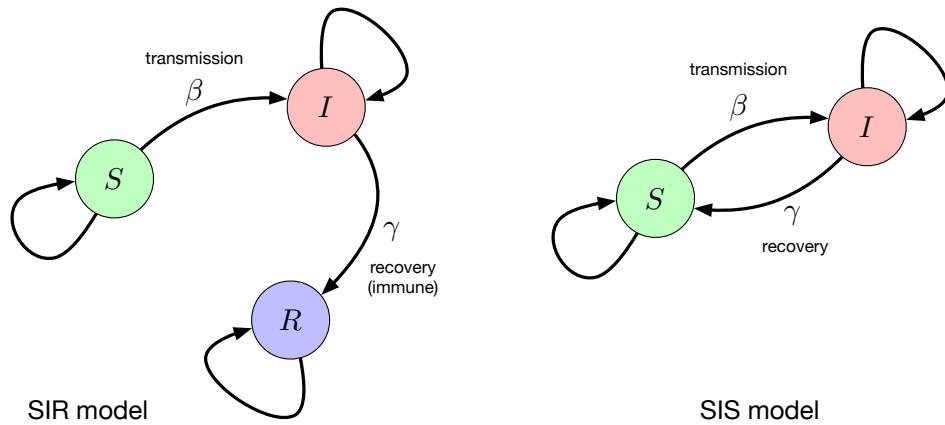
The **compartmental model** of an epidemic lacks any structure within its population. From a network perspective, we can imagine this model unfolding on a fully connected network, in which every person could be infected by, or could infect, any other person in the population. As a result, we might say the population is “well mixed.”

To answer questions at the population level, we need to model how individuals can change their “state” with respect to the spreading disease. In this simplest model, the network structure, such as it is, remains fixed, and each node has a **state variable** $x_i \in \{S, I, R\}$ or $x_i \in \{S, I\}$ that indicates which “compartment” a node is currently in.

The model's dynamics comes from defining a set of “transition” rules that describe how a node's state switches from one compartment to another. By tracking the counts of nodes in different compartments, we can track the evolution of an epidemic through the population. The basic compartmental model defines one compartment S for “susceptible” individuals, one compartment I for “infected” individuals, and, optionally, one compartment R for “recovered” individuals. Transitions among these compartments then define events like a susceptible individual becoming infected $S \rightarrow I$, an infected individual recovering with $I \rightarrow R$ or without $I \rightarrow S$ immunity.

The particular set of states and transition rules we choose defines our model of the spread of a disease. For instance, we might model the infection stage of an illness by using a sequence of “infected” compartments, e.g., $I_1 \rightarrow I_2 \rightarrow I_3$, which would represent a progression of a disease from one distinct stage to another. Similarly, there might be multiple types of susceptible states, capturing different kinds of susceptibility. This kind of flexibility means that there are *many different models* of disease spread, e.g., a model for how influenza spreads should be different from a model of ebola because these diseases spread through different means, and have different consequences on the hosts.

The most basic epidemiology models are the Susceptible-Infected-Recovered or SIR model and the Susceptible-Infected-Susceptible or SIS model, which have the following states and transitions:



- **SIS** can model diseases like influenza or the common cold, where recovery does not imply immunity (because there are other strains circulating).
- **SIR** is more realistic for diseases like chickenpox and measles, where recovery does imply immunity (because there's only one strain in circulation over the course of a human lifetime).

1.2 Specifying a SIR or SIS model

Both SIR and SIS models have parameters β , γ . These represent, respectively, the rate or probability of becoming infected, given an exposure, and the rate or likelihood of recovery, given an infection. The higher the value of β , the more likely an exposure leads to an infection. For instance, a highly contagious disease like measles will have a very high value of β , while something like the common cold will have a much lower value. Similarly, the higher the value of γ , the faster an infected individual recovers to become non-infectious again. The ratio β/γ provides a simple quantitative measure of the relative flow into the I compartment, and in the compartmental model,

it is equivalent to R_0 , which is defined as *the average number of secondary infections* per infected individual. The higher R_0 , the faster an epidemic will tend to grow.

1.2.1 Epidemic dynamics in SIS

The dynamics of the basic SIS compartmental model provide a reference point for our intuition about epidemic dynamics on a network. We can mathematically model the number of individuals in each of the two S, I compartment as follows. This model is a *continuous time* model, while in practice, network models are typically *discrete time* (with synchronous updates). More on that below.

- Let N be the total population (number of nodes), which we assume to be constant.
- An infected person infects some susceptible person with probability $\bar{\beta}$ per unit time.
- An infected person recovers, becoming susceptible again, with probability γ per unit time.
- Let $S(t)$ and $I(t)$ denote the number of susceptible and number of infected individuals, and note that $N = S(t) + I(t)$.

Now, consider how $S(t)$ changes over a small interval of time:

$$S(t + \Delta t) = S(t) - [S(t) \times \bar{\beta} \Delta t I(t)] + [I(t) \times \gamma \Delta t] . \quad (1)$$

Let's consider the structure of the equation:

- The first term is just the number of susceptibles we began with.
- The second term measures the flow of individuals out of the susceptible S compartment (and into the infected I compartment) due to new infections. This term is proportional to the product $S(t)I(t)$, because each susceptible is connected to every infected, and we assume that transmissions are independent (as in the configuration or Chung-Lu models).
- Finally, the third term measures the flow of individuals back into the susceptible S compartment (and out of the infected I compartment) due to recovery.¹

We can convert this difference equation into a differential equation by dividing S , I , and $\bar{\beta}$ by the population size N and unit time Δt , yielding

$$s = S/N \quad i = I/N \quad \beta = \bar{\beta}N \quad (2)$$

¹In the SIR model, this term would instead appear in the update equation for $I(t + \Delta t)$, because it represents the flow from I to R , the “recovered” (or “removed”) compartment.

and the rate equation for the number of infected individuals

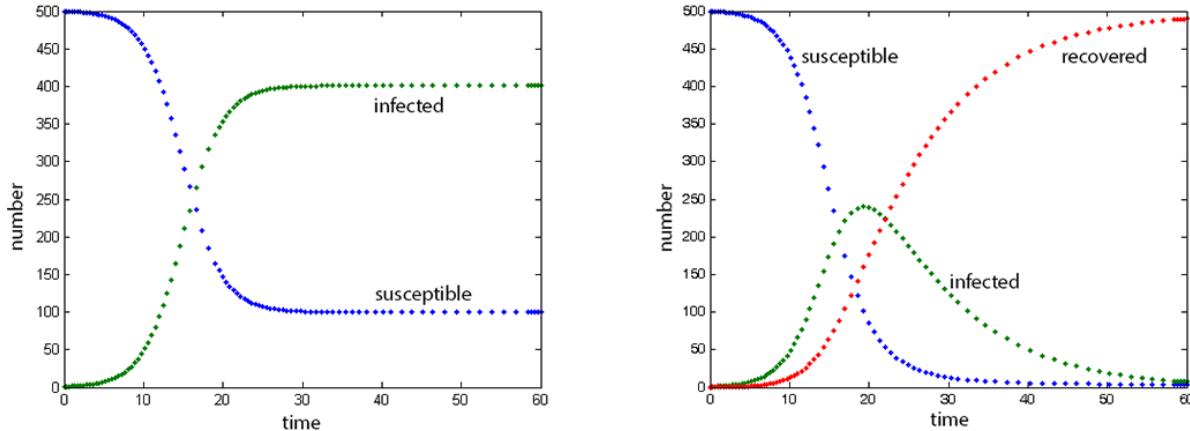
$$\frac{di}{dt} = \beta i(1 - i) - \gamma i . \quad (3)$$

We can use this equation to answer a simple question: will a new epidemic spread?

In the beginning of an epidemic, i will be very small (few individuals infected, relative to N), and we want to know whether and how it will grow. Under this assumption, we make the approximation $(1 - i) \approx 1$, which yields

$$\frac{di}{dt} \approx i(\beta - \gamma) . \quad (4)$$

This is an ordinary differential equation, whose solution is a *logistic function*, given a fraction i_0 of initially infected individuals. That means the initial growth of i is **exponential**, growing like $(R_0)^t = (\beta/\gamma)^t$, and when $\beta > \gamma$, an epidemic in the compartment model will tend to grow (exponentially) because the compartment I 's *rate* of in-flow exceeds its *rate* of out-flow. In contrast, when $\beta < \gamma$, the I compartment will tend to empty out more quickly than it fills up, and the epidemic dies out. When $\beta/\gamma = 1$, a value we call the **epidemic threshold**, we see wild fluctuations in whether the epidemic takes off or dies out.



1.2.2 SIS and SIR dynamics

The population's states S, I under the SIS model evolve like the figure above, on the left.² Because individuals can go back and forth between the two compartments, the relative proportion of indi-

²Adapted from: <https://en.wikiversity.org/wiki/File:Sissys.png>

viduals in each will eventually stabilize. The value it converges on is given by setting Eq. (3) equal to 0, and solving, which yields a steady state of $i \rightarrow 1 - \beta/\gamma$.

Under the SIR model, the population's states S, I, R evolve like the figure above, on the right.³ Based on the dynamics you see, what value do you think was chosen for the ratio β/γ ?

Initially, $I(t)$ grows exponentially in both cases. But, its behavior later differs—in the SIS case, the sizes of S and I eventually stabilize, at the point where the rate of infection $S \rightarrow I$ equals the rate of recovery $I \rightarrow S$. In the SIR case, the R compartment collects individuals over time so that eventually all individuals are either S (never infected) or R (all others recovered). As the fraction of individuals in S decreases, there are relatively fewer individuals to move to the I compartment, and this “emptying out” produces a characteristic peak in the $I(t)$ function. Because the early growth of $I(t)$ is exponential, the peak occurs sooner, and is reached more quickly, if $R_0 = \beta/\gamma$ is high, and the height of the peak is governed by the absolute value of γ , which determines how long an individual stays in the I state before transitioning to R . (Do you see why?)

1.2.3 Exponential growth in a real epidemic: covid-19

Exponential growth is *very fast*. A simple way to make this growth more intuitive is the “doubling time” of an epidemic: how many days τ (time steps) are required for the number of infected individuals to double, i.e., $I(t + \tau) = 2I(t)$? Because $I(t) \sim (R_0)^t$ early in the epidemic, we can calculate the doubling time no matter what value of t we choose. (Do you see why?)

The doubling time τ of a real epidemic depends on many factors, including the scale and type of public health response, the temperature sensitivity of transmission, etc., all of which can impact the observed R_0 . In the first few months of the covid-19 pandemic of 2020, the empirical doubling time varied across countries, but was roughly 3–4 days in most developed nations, including Italy, Spain, and the United States. Here are Italy’s early case numbers, from the World Health Organization:⁴

24 Feb.	27 Feb.	1 Mar.	4 Mar.	8 Mar.	11 Mar.	15 Mar.
124	400	1128	2502	7375	10149	21157

Over these 27 days, the case count increased by a factor of 170, which gives a doubling time of $\tau = (t_2 - t_1)/\log_2[I(t_2)/I(t_1)] = 3.64$ days. Were this rate to continue unabated, Italy would reach 3,600,000 cases a month later, and then over 14,000,000 a week after that. In the space of just 9 weeks, the epidemic would have spread to 24% of Italy’s population, killing 84,000 people (infected fatality rate of 0.6%). For reference, influenza kills about 17,000 Italians per year.

³ Adapted from: <https://en.wikiversity.org/wiki/File:Sirsyst-p9.png>

⁴ Data from the World Health Organization’s covid-19 Situation Reports:
https://en.wikipedia.org/wiki/Template:201920_coronavirus_pandemic_data/WHO_situation_reports

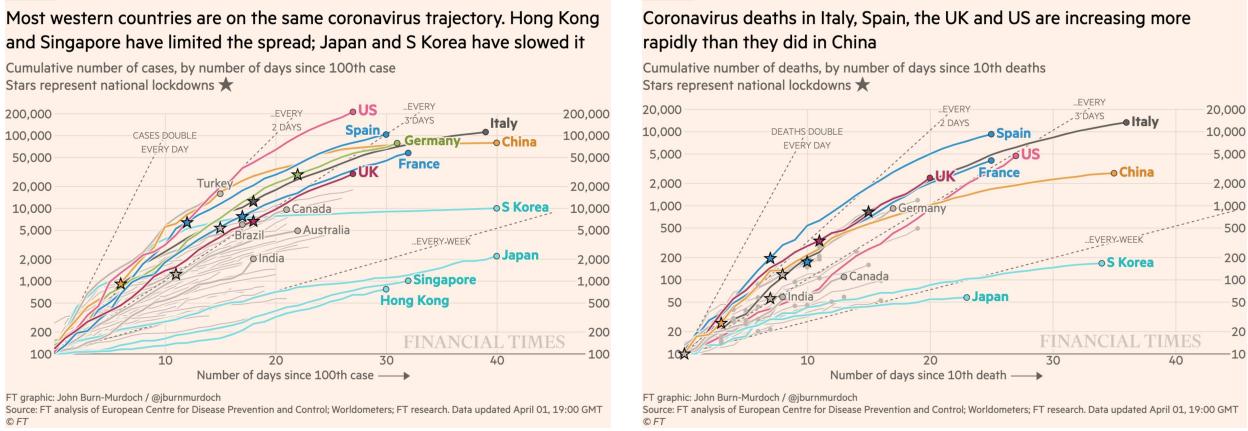
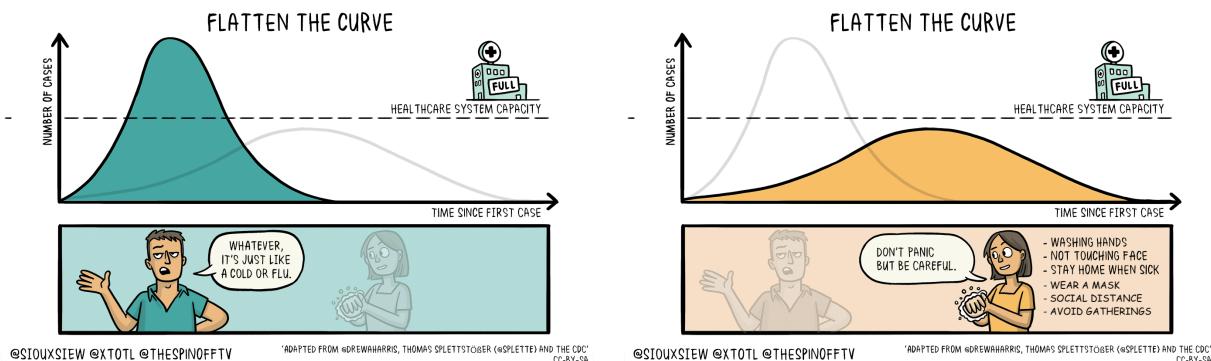


Figure 1: Official case and death counts, early in the covid-19 pandemic.

Of course, exponential growth cannot go on forever. The doubling time's utility as a measure of an epidemic's speed R_0 or its peak size $\max_t I(t)$ depends on how long the exponential growth holds. Population is an obvious long-term limiting factor: once a large fraction of the population becomes infected, the supply of susceptible individuals $S(t)$ is no longer large compared to the number of infected individuals $I(t)$, and the epidemic will begin to decelerate.

1.2.4 Flattening the curve

To limit the speed or peak size of an epidemic in the compartment model, we can change either β , the rate at which individuals become infected, or γ , the rate at which they recover. How much we can change either depends on the details of the pathogen and our public health system. For instance, in viral infections, like influenza and covid-19, where treatments are rudimentary, there are fewer things we can do directly to increase the recovery rate γ . In such a case, we instead focus our public health efforts on β , transmissibility. In contrast, in bacterial infections like *E. coli*, we can increase γ substantially, if a suitable antibiotic is available.



For a seasonal pandemic like influenza, a modern health care system tends to have enough capacity to provide adequate care to all individuals with serious cases: because it's seasonal and widespread, the peak number of cases is fairly predictable and treatment resources widely available.

However, if the health care system is overwhelmed by cases, i.e., $I(t)$ grows so rapidly that there are more serious cases than available hospital beds or intensive care units, this “collapse” of the health care system would itself cause γ to decrease (for all diseases), leading to many more deaths.⁵

In such an “explosive” pandemic situation, e.g., the covid-19 pandemic of 2020, a good public health strategy aims to “flatten the curve” (see cartoon above, from March 2020, which predates the understanding that wearing a facial covering also lowers β). By lowering β , we aim to *slow* the exponential growth of $I(t)$ so that it peaks lower (ideally, low enough that it is below the health care system’s capacity) and later, so as to buy time for the development of novel treatments (vaccines, etc.) and the construction of adequate resources (more ICUs, etc.). At worst, these actions won’t change the total number of infections over the epidemic, but by prolonging its duration, the health care system is better able to keep up with the peak case load, keeping γ high for all cases (including other medical needs, e.g., broken bones, cancer, etc.), and more time is created to find effective medical treatments or management strategies.

A key strategy to flatten the curve is “social distancing,” a kind of network intervention, in which we modify the contact network the disease exploits so that fewer secondary cases are produced by every new infection. Social distancing explicitly targets the exposure network G in order to lower R_0 and decelerate the exponential growth. We’ll discuss this idea in more detail later.

1.3 Epidemics on a network

The difference between a compartment model and a network model of an epidemic is that the network allows us to explicitly capture the way individual social interactions enable a pathogen to spread. The compartment model assumes that every individual can infect any other individual in the population, but this is unrealistic—we can only be infected by those we interact with, and we don’t interact with everyone. The network allows us to better capture the structure of these interactions and explore how network structure shapes an epidemic.

We begin by answering the two fundamental questions for using a network $G = (V, E)$ in this setting: *What are nodes? And, what are edges?*

⁵In such a case, doctors will likely be forced to ration life-saving resources using “wartime” triage protocols. Such a situation occurred in both Italy and Arizona during the covid-19 pandemic:
<https://www.theatlantic.com/ideas/archive/2020/03/who-gets-hospital-bed/607807/>.

Typically, nodes are individuals (humans or animals), and edges are potential exposures. Two nodes i, j are only connected if i can expose j to an illness. If not, then there cannot be an edge between i, j . Hence, different modes of exposure define different kinds of networks.

The first is the *exposure network* G , in which edges are defined by the potential for an exposure to a pathogen between two nodes i and j . For example, where are several different ways we could define an exposure interaction:

- close proximity (influenza, common cold)
- physical contact with a fomite (inanimate object harboring live pathogen, e.g., pink eye)
- physical contact with fluids (STDs)
- contact with an animal vector (mosquitos and malaria).

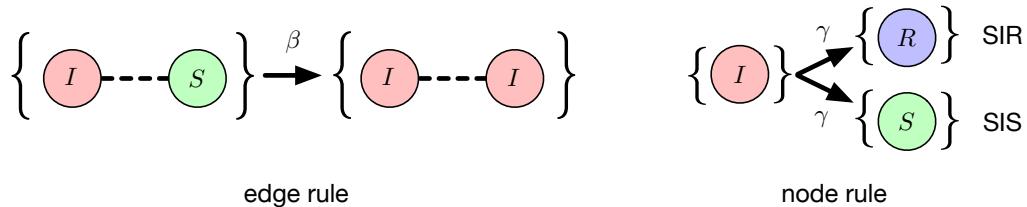
But not all potential exposures result in actual *transmissions*. The second network we define is the network of actual transmissions $G_T = (V, E_T)$, whose edges E_T are a subset of the potential exposures $E_T \subseteq E$. In the transmission network, every edge represents a *directed* transmission, in which j became infected by its interaction with i . If infection events are unique for an individual (as in SIR), then edges are directed and G_T is always a tree, whose root is the “patient 0” of the epidemic.

The meaning of R_0 , the average number of secondary infections, is exactly equal to the average out-degree $\langle k^{\text{out}} \rangle$ of the transmission network G_T . Thus, R_0 is not an intrinsic property of a pathogen. Rather, R_0 is an observed pattern describing the average manner a particular pathogen spreads through a particular human population. The idea of “flattening the curve” is, in fact, the idea of modifying the exposure network in order reduce R_0 .

1.3.1 Dynamics on the network

Because not every susceptible individual connects to every infected individual, the structure of the potential exposure network G shapes both which and when nodes get infected.

In the simplest network epidemiology model, time progresses synchronously in discrete steps. To manage the transitions of nodes from one state $x_i(t)$ to another $x_i(t+1)$, we define a set of update rules for the network, one for the edges, and one for the nodes:

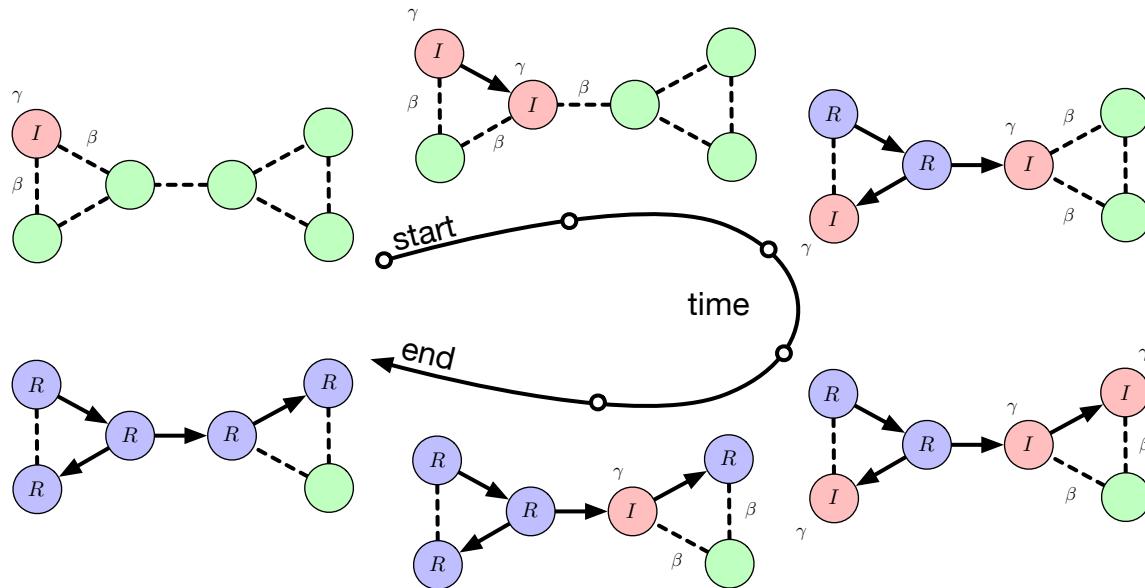


The conceptual meanings of β and γ here are the same as in the compartment model, but mathematically, their meaning have changed slightly. Here, when we find a motif of the form on the left, we transform it into the motif on the right with probability β for an edge update (transmission) and γ for a node update (recovery). Hence, β in a network model is the independent probability that an exposure leads to infection, and γ is the independent probability that an infected node recovers.

The conceptual meaning of R_0 is also the same as in the compartment model: it denotes the expected number of secondary infections. But, in a network model, R_0 is related to $\beta \times \langle k \rangle$, i.e., both the transmission probability *and* the network structure govern R_0 . That means an epidemic can spread faster by increasing either its transmissibility *or* the density of connections. Thus, R_0 is not an intrinsic property of a disease, and instead it depends both on how easily humans transmit the disease to one another (β , which can be modified by hygiene, demographics, etc.) and on how many opportunities an infected human has to spread it ($\langle k \rangle$, on average, which can be modified by social structure, lifestyle, etc.), both of which can change over time or context.

1.3.2 An example on a network

Given a network where some node is the initial infection (the “patient 0”), we can apply the rules to simulate the spread of the infection across the network. The simulation halts when there are no infected nodes. In the example below, edges in the potential exposure network G are dashed, while edges in the transmission network G_T are solid.

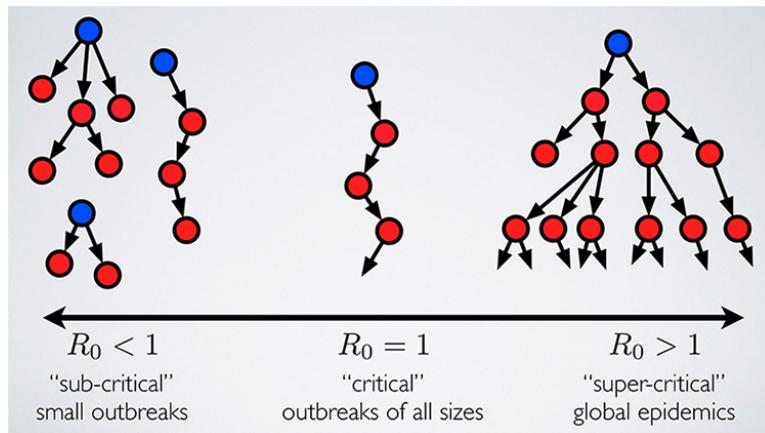


At the end of this epidemic, there is only one node (bottom right) that escaped infection entirely. The bottom-left node could have been infected by either of its neighbors, but only one of those edges is included in the final transmission network.

1.3.3 The role of R_0

The basic reproduction number R_0 plays a critical role in giving us a sense of what kind of an epidemic an infection will produce. Remember that in the network, $R_0 \approx \beta \times \langle k \rangle$, meaning that we can increase it by either increasing the transmission probability or increasing the network's connectivity.

When it is below the epidemic threshold, the transmission graphs (trees) tend to be small. Above the threshold, and the expected number of additional infections is greater than 1, which implies an exponential growth process (consider $R_0 = 2$; what kind of a tree does this create?) that will eventually consume every node reachable from the initial infection. At the critical value of $R_0 = 1$, we get outbreaks of all different sizes.

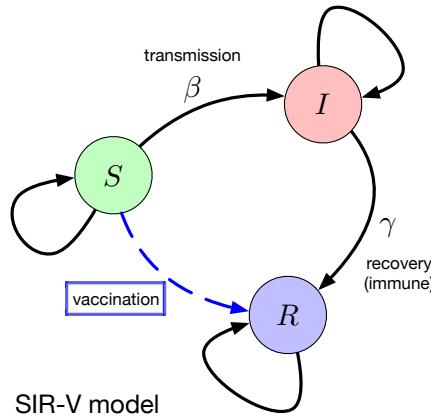


In fact, we've seen (mathematically) exactly this behavior before! It was in the *phase transition* in the size of the giant component for the Erdos-Renyi random graph model $G(n, p)$ in Lecture 3. Look back at the figure that visualized ER graphs for different choices of mean degree $c = \{0.5, 1, 2, 4\}$. There, the mean degree c plays exactly the same role as R_0 here.

1.4 Stopping an epidemic on a network

Vaccination is a remarkably achievement of public health: for most people, it provides a means to transition from a susceptible state S to a “recovered” (immune) state R , without having to go

through the experience of being infected I .



This is useful for individuals, but also useful for the population, because placing an individual into the R state effectively deletes their edges from the potential exposure graph G . And, deleting many edges from G necessarily reduces the mean out-degree R_0 in the transmission graph G_T , and, ideally, moves it below the critical threshold of $R_0 = 1$. That is, vaccinations break up the network into small, disconnected components, any one of which could host a small epidemic, but such an outbreak cannot spread to the other components. Vaccination thus protects the rest of the network, and this is called **herd immunity**.

The higher the value of R_0 for a disease, the greater a fraction of the population needs to be vaccinated in order to push the transmission graph below the critical threshold. Here are some examples of R_0 values:

disease	R_0	transmission	vax.	data from
measles	12 – 18	airborne	90–95%	1912-1928 in US + 1944-1979 in UK
chickenpox	7 – 12		85–90%	
polio	5 – 7	fecal-oral route	82–87%	
small pox	1.5 – 20+	airborne droplet	70–80%	
H1N1 flu	1 – 3	airborne droplet		
ebola	1.5 – 2.5	bodily fluids		
zika	2			
covid-19	≈ 2.4	aerosols	60–85%	

The data for the R_0 values is empirical, as the example of measles illustrates. That means that the value of R_0 for a particular disease depends on the current structure of human social organization and human behavior. The better the public health system, and the more isolated individuals are from each other, the lower the R_0 will be, even for the same disease.

1.4.1 Network strategies for targeted vaccination

Suppose we had only a limited supply of vaccines, but we still wanted to stop an epidemic. The limited number means we cannot rely on the classic vaccination strategy of “vaccinate everyone who isn’t immuno-compromised.” Instead, we can try to exploit the network structure itself, by vaccinating nodes that would either *slow down* the epidemic (making it take longer paths through the network) or *break up* the network into smaller components.

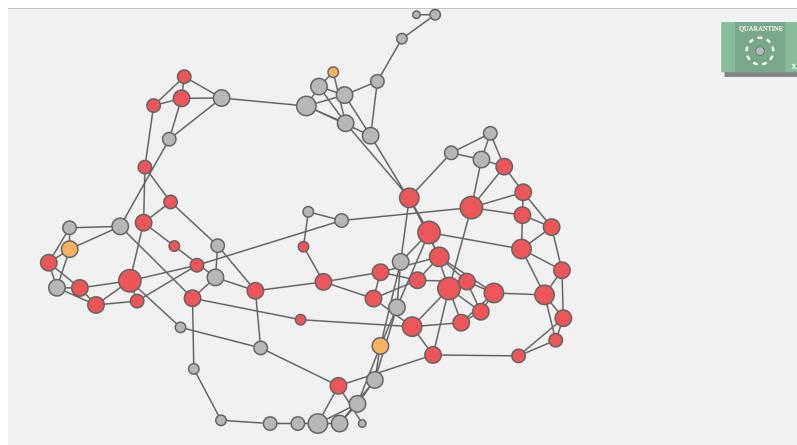
Here are some possible strategies:

- vaccinate by node attributes, e.g., the young and old (who are less likely to survive a bad infection)
- vaccinate randomly
- vaccinate higher-degree nodes first, e.g., teachers, doctors, service industry workers, etc.
- vaccinate “bridges” that link different social communities

1.4.2 Try your hand

Prof. Marcel Salathe’s group at EPFL in Switzerland has created a web game that challenges you to precisely the above problem: can you stop an outbreak through targeted interventions?

Try it out here: VAX! <https://vax.herokuapp.com>. The screenshot shows an example of an ongoing outbreak on a small social network.



1.5 Modeling Epidemics on Networks

There are several useful Python packages for modeling epidemics on networks:

- **Epidemics on Networks** (EoN) is a package for simulating SIS and SIR models on networks. EoN works on top of `networkx`, and allows event-based simulations on simple or weighted networks, synchronous updating, and visualization of the epidemic results, e.g., epidemic trajectories like $I(t)$.

Highlights and tutorial: <https://epidemicsonnetworks.readthedocs.io/en/latest/>

- **SEIR+ Model** is a package for simulating SEIR models on networks, where the E state represents individuals who are “exposed.” SEIR+ also works on top of `networkx`, and includes additional states and transitions in order to model an epidemic like SARS-CoV-2, where testing and latent infections play a substantial role in the epidemic’s trajectory.

Highlights and tutorial: <https://github.com/ryansmcgee/seirsplus>

Supplemental readings

1. van den Driessche, “Reproduction numbers of infectious disease models.” *Infection Disease Modeling* **2**, 288–303 (2017)
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6002118/>
2. Delamater et al., ”Complexity of the Basic Reproduction Number R_0 .” *Emerging Infectious Diseases* **25**(1), 1–4 (2019)
<https://www.ncbi.nlm.nih.gov/pubmed/30560777>
3. Bansal, Grenfell, and Meyers, ”When individual behaviour matters: homogeneous and network models in epidemiology.” *J. Royal Society Interface* **4**, 879–891 (2007)
<https://royalsocietypublishing.org/doi/full/10.1098/rsif.2007.1100>