

## 1 Network Epidemiology: Models and Complications

In this lecture, we will explore more deeply how network structure can drive more complicated and more realistic dynamics in the evolution of epidemics.

### 1.1 Epidemic models with structure

Simple epidemic models running on uncomplicated networks produce simple epidemic dynamics. These tend to look like

1. a single exponential growth phase at the beginning of the spread,
2. a single peak, and
3. either a steady state (SIS) or a single fall back to the baseline (SIR).

Varying the degree structure, or even the density of triangles, or even introducing simple forms of community structure, does not change this pattern much. It may broaden or sharpen the single peak, but the single-peak pattern remains. However, when we look at the dynamics of real epidemics, we see far more complicated behaviors, and shown in Fig. 1 below.

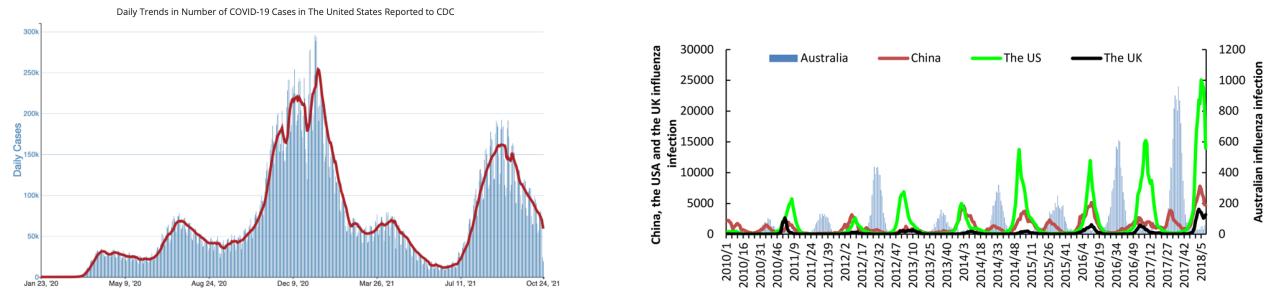


Figure 1: (left) COVID-19 case time series for the U.S. from January 2020 to October 2021, as recorded by the U.S. Center for Disease Control, showing five distinct “waves” of cases. Reproduced from the CDC COVID Tracker. (right) Influenza (all strains) case time series for four countries from 2010–2018, showing annual waves of different sizes, which oscillate between northern and southern hemisphere countries. Reproduced from Zhang et al. (2019).

There are many specific reasons why real epidemics have more irregular shapes or even run in wave-like dynamics, with multiple peaks, and different rates of increase or decrease. Recall that the dynamics of an epidemic depend on both (i) the biology of transmission and recovery (modeled by  $\beta$  and  $\gamma$ ) and (ii) the shape of the exposure network  $G$ , where we assume that edges are the mechanisms of transmission.

Hence, from the perspective of network epidemiology, irregular epidemic dynamics must be driven by one or the other of these two parts of the model.

- Changes in either the basic transmissibility of the pathogen  $\beta$  or the recovery rate  $\gamma$  can increase or decrease the rate of spread, even with a fixed exposure graph.

These changes could be driven by evolution of the pathogen itself, as in the shift from the wildtype SARS-CoV-2 virus to the alpha variant and then to the delta variant over the first 18 months of the COVID-19 pandemic,<sup>1</sup> or in the way the environment interacts with transmission, e.g., because of changes in humidity or temperature, or by changes in medical interventions, such as improved treatments.

- Changes in the network of exposures  $G$ , driven by the dynamics of the social contact network.

These changes can be caused by any number of things that shape who contacts with whom in our social world. A few examples with known relevant to disease spread include (i) time-varying adoption rates of non-pharmaceutical intervention (NPI) behaviors like social distancing, mask wearing, hand washing, self-quarantining, economic closures, etc., (ii) environmental influences, such as seasonal temperature changes, and (iii) even by the opening up of new venues for social contact, such as in opening a new transportation link between two places or opening up a new concert venue.

Here, we will explore the second category, in which the structure of the network shapes the dynamics of the spread itself to ensure that *the epidemic doesn't happen everywhere at the same time*.

### 1.1.1 Hierarchically structured populations

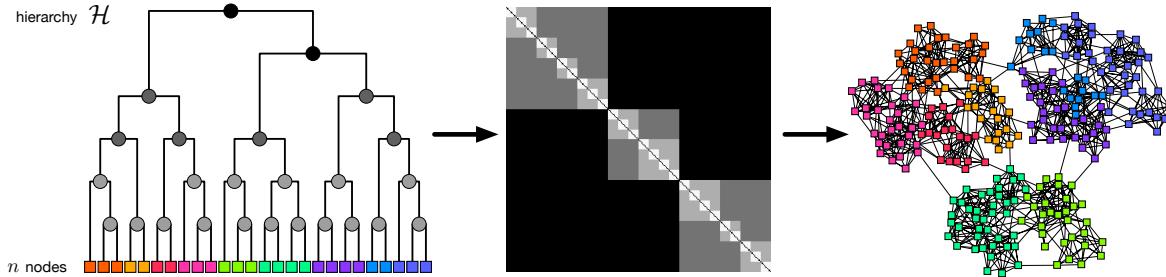
Real social networks are very, very large. At this scale, there's plenty of room for multiple levels of structural patterns, and we can model these via "hierarchical" structure, in which nodes tend to divide into groups that further subdivide into groups of groups, and so forth over multiple scales—nations, regions, cities, towns, neighborhoods, and households, or loose associations and the many smaller, closer groups they are composed of. This kind of hierarchical structure can appear for many different reasons, and is a good general way to represent multi-scale structural patterns in networks.

We typically represent the hierarchical organization of a network using a tree or a dendrogram  $\mathcal{H}$ , in which the nodes of the network are the leaves of the tree, and the internal branches show how we divide things into progressively smaller groups, as we move down the hierarchy from the whole system to its components.<sup>2</sup> The "group" that two nodes  $i, j$  belong to is the one defined by their lowest common ancestor in the hierarchy. Hence, the higher up in the hierarchy the lowest common ancestor, the more leaf nodes are below it and the larger the group it represents.

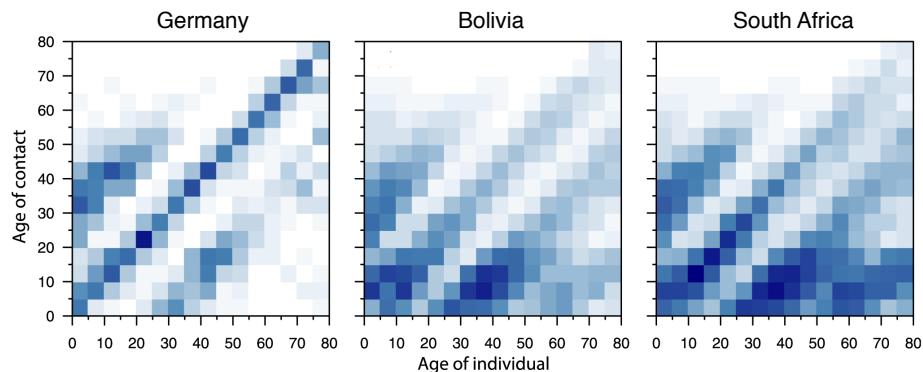
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<sup>1</sup>To say nothing of the omicron variant and its enormous wave, which epidemiologists estimated infected roughly 40% of the U.S. population in the space of about 10 weeks, from December 2021 through mid February 2022.

<sup>2</sup>Binary trees are a convenient choice for hierarchical structure, but any type of tree suffices.



We can turn a hierarchy of groups  $\mathcal{H}$  into a network model by defining the probability that two nodes  $i, j$  are connected to be proportional to their “relatedness” in the hierarchy, where nodes with a smaller distance on the tree (lower common ancestor) are more related.<sup>3</sup> This assumption produces assortative “nested” communities, because the within-group density of edges increases as we consider smaller groups (moving down the hierarchy; see figure below). This pattern models the idea that you are more likely to interact with someone who lives in your neighborhood, or takes a class with you, or belongs to the same social organizations, than with someone who lives far away, or has divergent social interests.



One particular kind of large-scale population structure that we can model as a kind of hierarchy is an *age-structured population*, where most people interact with others who are within about 5 years of their own age, and they interact at slightly lower rates for people within 5–10 years of their age, etc.<sup>4</sup> The exception to this pattern comes from families: children interact at high rates

<sup>3</sup>See Clauset, Moore & Newman, “Hierarchical structure and the prediction of missing links in networks.” *Nature* **483**, 98 (2008) for more details of how this model works.

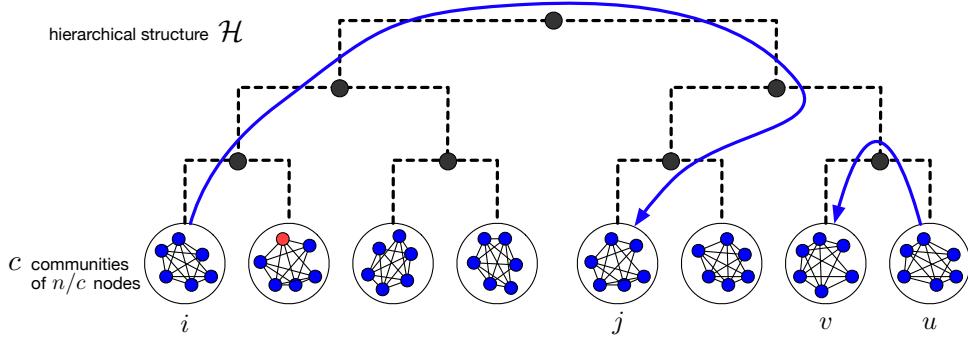
<sup>4</sup>Figures from Prem, Cook & Jit, *PLoS Comp. Bio.* **13**, e1005697 (2017)  
<http://dx.doi.org/10.1371/journal.pcbi.1005697>.

with individuals about 25–35 years (and about 60 years) older than them, which creates strong but specific off-diagonal patterns in the mixing matrices. On this kind of network, how would an epidemic spread? What prevents the epidemic from being everywhere at the same time?

### 1.1.2 Epidemics on hierarchical networks

The effect of hierarchical structure on epidemics is to prevent the epidemic from happening everywhere at once, and instead allowing it to repeatedly find naive subpopulations that together produce the ups and downs of realistic case counts. But rather than model the hierarchical network explicitly, we can capture its implicit structure using a hierarchical metapopulation simulation.<sup>5</sup>

To begin, we create  $c$  communities, and populate each with  $n/c$  nodes. Each of these communities will run its own SI-X compartment model, meaning that we assume each community is itself well mixed, with a common choice of  $\beta$  and  $\gamma$  parameters. Initially, all nodes are in the  $S$  state, and we infect a single node  $x_r = I$ , chosen at random. Then, with probability  $p$ , at each step of the model, each node relocates from its current community  $i$  to another community  $j$  chosen with probability  $q_{ij} \propto e^{-\lambda d_{ij}}$ , where  $d_{ij}$  is the tree distance between  $i$  and  $j$ .<sup>6</sup> The simulation then runs until the epidemic ends, or for as long as we like.



In this model, the parameter  $p$  acts like a global mixing rate, as it determines the frequency at which nodes relocate to different communities. When  $p$  is small, the community-level epidemics remain relatively independent, but once  $p$  is above some threshold, a local epidemic will tend to

<sup>5</sup>This model was first described and explored in Watts et al., “Multiscale, resurgent epidemics in a hierarchical metapopulation model.” *Proc. Natl. Acad. Sci. USA* **102**, 11157 (2005).

<sup>6</sup>We can efficiently calculate a distance  $d_{ij}$  by assigning a binary string of length  $\log_2 c$  to each community (and hence to all nodes in that community), where each string encodes the sequence of left (0) or right (1) moves on the hierarchy, traversing from the root down to that community. Then, the tree distance  $d_{ij}$  for communities  $i$  and  $j$  is simply the edit distance or L1 norm of the two strings. In the figure here, community  $i$  would have label 000,  $j$  would have label 100,  $u$  label 111, and  $v$  label 110. If the hierarchy is a  $b$ -ary, meaning each branch has  $b$  children, then we use a  $b$ -ary string of length  $\log_b c$ .

export infected individuals to other communities, allowing it to spread globally. In contrast,  $\lambda$  sets the scale of that spread by tuning the typical distance over which a node will tend to relocate. When  $\lambda$  is large, nodes relocate to more nearby communities, and when  $\lambda$  is small, nodes tend to travel further. In the figure above, we have a depth 3 binary tree as the hierarchy on a set of 8 communities, and two relocations are shown as blue arrows: one long jump, and one short jump.

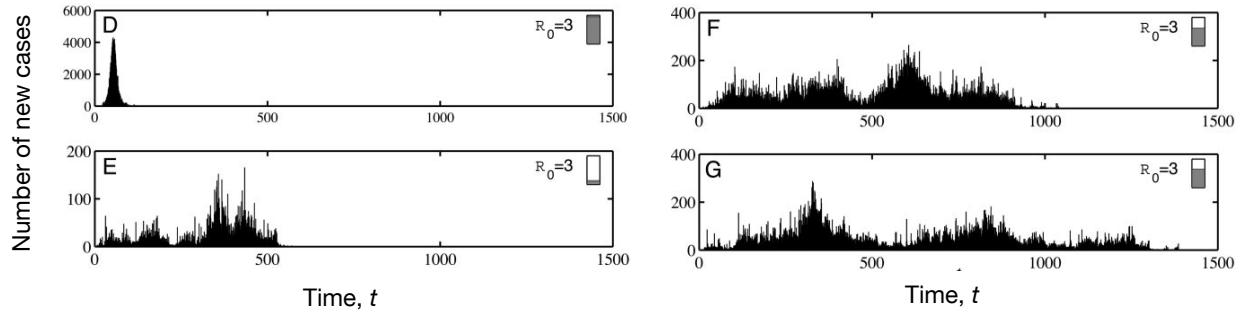


Figure 2: Simulated new case counts  $\Delta I(t)$  over time, for the hierarchical metapopulation model with  $n = 102,400$  nodes and  $\beta/\gamma = 0.3/0.1 = 3$ . (D) No hierarchy, only a single large community, showing classic SIR dynamics. (E-G) Hierarchy, with a  $b = 4$  branching ratio in a tree with depth  $\ell = 5$  and  $n/c = 100$  nodes in each of the  $c = 1024$  communities, showing complicated dynamics of repeated resurgence. Adapted from Watts et al. (2005).

The epidemic dynamics produced by this model are far more realistic than the classic SIR model (see Fig. 2), reflecting the fact that the spreading process continually seeds epidemics in naive (still susceptible) subpopulations of different sizes. Each “resurgence” of the case numbers corresponds to such a new local epidemic starting up, and if we marked along the time axis the times at which an infected individual relocated to a previously fully susceptible community, these marks would line up with the upward swings of the curve. Within the model, the parameters  $p$  and  $\lambda$  ultimately shape the speed and scale at which the epidemic spreads across communities, and tune how densely or sparsely spaced out these new local epidemics are.

### 1.1.3 Real-world hierarchical structure

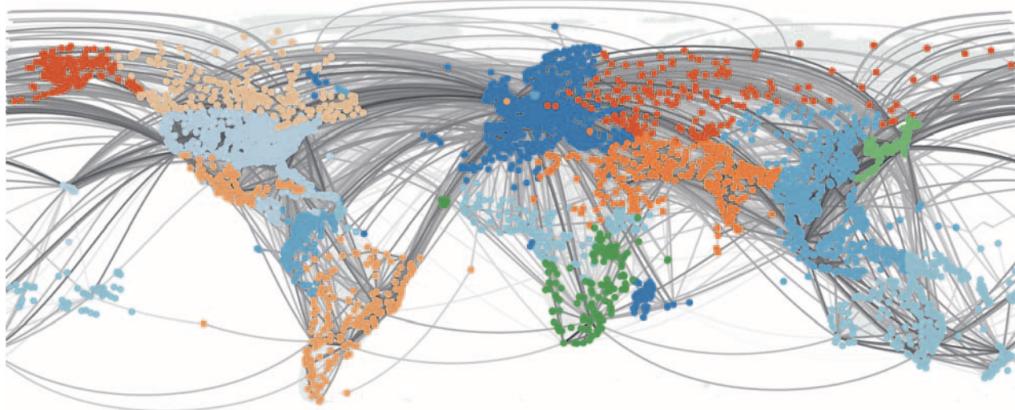
Large-scale transportation networks, such as roads, trains, and airplanes, have an explicit hierarchical structure because humans tend to engineer such systems in this way.<sup>7</sup> Roads are arranged in major and minor highways, main arteries, all the way down to side streets, and the larger the road,

<sup>7</sup>Of course, scientists have all sorts of explanations for why this is the case. Some have to do with the clumpiness of humans in space, which may follow a fractal-like pattern; another explanation says that self-similar clumpiness just follows the fractal-like structure of the natural environment. Other explanations argue that hierarchies provide certain kinds of efficiencies and robustnesses to perturbations.

the more traffic it carries and the more distance locations it tends to connect. Train, shipping, and air travel networks all have similar structure.<sup>8</sup>

For understanding the global dynamics of pandemics, like influenza and COVID-19, we must focus on transportation at the global scale, which means mainly air travel. Here, nodes are airports, and two airports are connected by a directed edge with weight  $w_{ij}$  equal to the mean number of daily passengers that fly from airport  $i$  to airport  $j$ , and this network plays the role of the hierarchy  $\mathcal{H}$  in our metapopulation model, by governing the way individuals relocate from one community (city with an airport) to another.

The structure of the global air travel network is well-studied, and exhibits many of the very same statistical patterns we see in other real-world networks: a heavy-tailed degree distribution, community structure, and triangles. On top of these patterns, the network is spatial, because nodes (airports) are embedded in a 2-dimensional space, the surface of the Earth.<sup>9</sup>



Empirically, the probability that two airports are connected decreases exponentially with the spatial distance that separates them, modulo some complexities that come from the spatial arrangement of landmasses on the surface of the Earth. We can see some of these features in the figure below, which shows 4069 airports worldwide, along with the corresponding edges. In this network, the largest-degree nodes, like London Heathrow (UK), Guangzhou China, Atlanta GA, and Denver CO are also the most central, with the most flights passing through them and having the smallest number of hops from them to any other airport in the system. Hence, traveling from an airport  $i$  to some other airport  $j$ , is likely to go “up” in the hierarchy of airports, toward the more major

<sup>8</sup>For an excellent review of the shape of real-world transportation networks, see Barthélémy, “Spatial networks.” *Physics Reports* **499**, 1–101 (2011).

<sup>9</sup>From Brockmann and Helbing, “The Hidden Geometry of Complex, Network-Driven Contagion Phenomena.” *Science* **342**, 1337 (2013).

hubs, and then back down to more local airports for the final step. This pattern is very much like navigating the road network, where crossing larger distances in space typically requires using “larger” roads.

The insight that the air travel network is a mechanism that relocates individuals from one “community” to another, at the global scale, suggests that we can replace the abstract hierarchical structure  $\mathcal{H}$  in our metapopulation model with the airport network itself. This change yields a more realistic model of the global spread of a pandemic, and allows us to examine how proximity in the airport network can increase the risk of disease importation. It does not tell us how epidemic dynamics below this level of representation might feed into or be driven by the dynamics at this global scale, but one could imagine replacing the SI-X model within each community with a more fine-grained network model that captures the particular age or population structure of that community.

In a 2013 paper, Brockmann and Helbing constructed precisely this kind of air travel-based hierarchical metapopulation model.

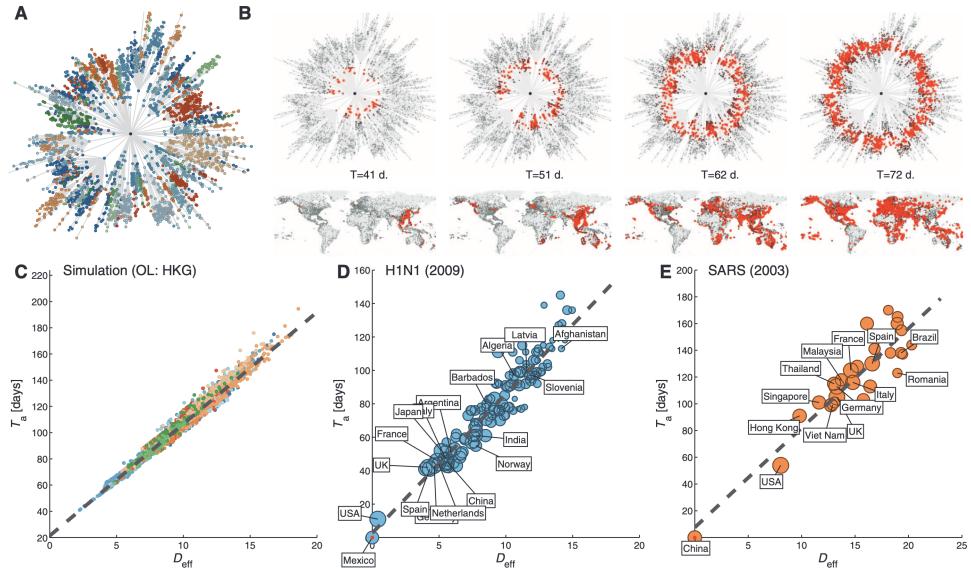


Figure 3: (A) The shortest-path tree from the Hong Kong airport (HKG), where radial positions are correspond to effective distances  $D$ , and node color follows the network figure above. (B) Simulated propagation waves of infection, spreading outward from HKG. (C) Simulated “arrival times” of the epidemic as a function of total effective distance from HKG. (D, E) Empirical arrival times of two pandemics (H1N1 in 2009 and SARS-CoV-1 in 2003) as a function of total effective distance from their points of origin; the excellent agreement between simulation and data here suggests that the global spread of these two pandemics was largely driven by the airport network’s structure. Reproduced from Brockmann & Helbing (2013).

Their key insight was that some edges in the airport network carry far more passengers than others, and hence that link is more likely to transfer an infected individual from one community to the other. To parameterize their hierarchy, they first computed the fractional average flow of daily passengers  $w_{ij} = f_{ij} / \sum_j f_{ij}$ , where  $f_{ij}$  is the mean number of daily passengers  $f_{ij}$  flowing from node  $i$  to node  $j$ . These flows could be used to determine a particular individual's trajectory through the network, e.g., by interpreting these weights as probabilities in a first-order Markov chain. But, to understand how the structure of the flows overall shape an epidemic, they instead used them to calculate a pairwise distance matrix  $D$ , where  $D_{ij}$  is the total “effective distance” of the edges in a geodesic path from  $i \rightarrow j$ , where the effective distance of an edge is defined as  $d_{ij} = (1 - \log w_{ij})$  (do you see why this transformation is reasonable?).

From this perspective, we now have an effective hierarchy  $\mathcal{H}$ : an infected individual is more likely to transit between airports with smaller effective distance  $D$ , implying that these airports are closer together in the hierarchy. Running a standard SIR epidemic over this structurally-parameterized hierarchical metapopulation model produces remarkably realistic simulations of how real pandemics have spread, such as the H1N1 flu in 2009 and the SARS-CoV-1 in 2003 (see Fig. 3), with the arrival time of the epidemic correlating very strongly with the effective distance between the source and the arrival point within the implied airport network hierarchy.

## Supplemental readings

1. Watts et al., “Multiscale, resurgent epidemics in a hierarchical metapopulation model.” *Proc. Natl. Acad. Sci. USA* **102**, 11157 (2005)  
<https://www.pnas.org/content/102/32/11157>
2. Brockmann and Helbing, “The Hidden Geometry of Complex, Network-Driven Contagion Phenomena.” *Science* **342**, 1337 (2013)  
<https://www.science.org/doi/10.1126/science.1245200>
3. Monod et al., “Age groups that sustain resurging COVID-19 epidemics in the United States.” *Science* **371**, eabe8372 (2021)  
<https://www.science.org/doi/10.1126/science.abe8372>
4. Mistry et al., “Inferring high-resolution human mixing patterns for disease modeling.” *Nature Communications* **12**, 323 (2021).  
<https://www.nature.com/articles/s41467-020-20544-y>