



# SFI TRANSMISSION

## COMPLEXITY SCIENCE FOR COVID-19

**STRATEGIC INSIGHT:** The disease models used to guide policy for the COVID-19 pandemic must capture key complexities of transmission.

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The study of infectious disease dynamics can be divided into two areas. The first is pathology, which focuses on changes in the hosts due to the presence of the pathogen (e.g., dry cough, high fever, and acute respiratory syndrome). The second is transmission, or how the pathogen moves from an infected individual to an uninfected one in order to initiate a new infection. In sharp contrast to pathology, we almost never see transmission occurring — we can only infer that it has occurred when a healthy individual develops signs of infection. We then need to trace back their activities in the hopes of identifying an individual with symptoms that led to the transmission event.

This post will supply an overview of the problems that beset epidemiologists when we try to measure transmission, while familiarizing the reader with some key models used to measure transmission, and to prevent it.

Models that are used to describe the dynamics of infectious diseases fall into four broad categories:

- microparasites and macroparasites;<sup>1,2,3</sup>
- vector-borne diseases (VBDs);
- sexually transmitted diseases (STDs); and
- other infectious diseases (OIDs).<sup>4</sup>

An overview of the first three categories appears in the [extended version of this post](#). For the purpose of understanding SARS-CoV-2, the virus that causes COVID-19, we shall jump to the fourth category — Other Infectious Diseases (OIDs).

OIDS are transmitted by free-living particles, expelled from the infectious hosts, that directly infect the susceptible hosts. The duration of time these infective stages last in the free-living stage is crucial — in the case of influenza and SARS-CoV-2, coughing and sneezing release a cloud of infective particles into the air that may only be infectious for a couple of minutes. In contrast, bacteria such as anthrax produce spores that

may survive in the soil for decades. The parasitic worms that live in the guts of most vertebrates produce eggs that can survive for weeks to months. This creates a bifurcation in transmission mode; when infectious stages are short-lived, then transmission from one infected individual is a function of the density of susceptible hosts in their vicinity. You infect many more people when you sneeze in a crowded subway car than when you sneeze in a nearly empty one. This form of transmission, usually called density-dependent transmission, is assumed to be linear, with each infected individual infecting a fixed proportion of the susceptible individuals in their vicinity. In contrast, pathogens with long free-living stages, as well as vector-borne pathogens and STDs, tend to have saturating transmission functions: mosquitoes have to digest between blood meals, and even Casanova had to rest or dine occasionally. This form of transmission is modeled by frequency-dependent functions with the product of susceptible and infected hosts appearing in the numerator, and the total population in the denominator.

The shotgun splatter of direct transmission is not very specific. Occasionally, the pathogen infects the wrong host — this can occur when different species are forced to interact artificially when captured for food or the pet trade. These animals are often stressed, which leads them to release significant numbers of infective stages that can contaminate humans involved in the trade. Usually, the pathogen is unable to survive in the new hosts, as the cells it needs to infect in order to replicate are absent. However, when a pathogen does manage to infect novel cells, it can lead to the emergence of a new disease. This seems to be what is happening with COVID-19. Genetic evidence suggests its natural host is a bat species,<sup>5</sup> or possibly a pangolin. These species have very different physiology from humans (and most of our domestic livestock species); we rarely see any overt pathology in bats infected with these pathogens. This can change dramatically when the pathogen finds itself in the wrong host.

Bats have very different immune systems from other mammals, likely as a consequence of their ability to fly.<sup>6,7</sup> Humans and other non-volant mammals produce the B-cells of their immune system in their bone marrow. Because bats fly, they have hollow bones; the only place they have bone marrow is in their pelvises, so they produce B-cells at much lower rates. Similarly, active flight raises their body temperature to levels akin to fever in non-volant mammals, possibly constraining viral growth. Bats also do not store fat, as it compromises their aerodynamic ability. Instead, they can enter torpor to get through periods of limited food resources. These all act as constraints on viral pathogens that disappear when the pathogen finds itself in a novel host whose immune response may interact with that pathogen in ways that are detrimental to both the host and the pathogen.<sup>8</sup>

The dynamics of generalist pathogens provide important insights into the transmission dynamics of pathogens in structured human populations. Consider a pathogen that can infect multiple host species, each of which has a different body size, and thus different

birth and death rates and population densities. The species with the smallest body size will have the highest birth and death rates and population density. The largest will have the opposite. If the pathogen follows simple dynamics, with within-species transmission far exceeding between-species transmission, then each host will interact independently with the pathogen and each will exhibit its own epidemic cycles: large and frequent outbreaks in hosts with low body mass, and slow, less dramatic cycles in larger hosts.<sup>9</sup> As we increase the relative rates of between-species transmission, these cycles will die out. Additionally, any tendency for epidemic outbreaks to occur is buffered by the pathogen's constant jumps between host species, preventing any one species from becoming too abundant. If we increase between-species transmission to levels where it matches within-species transmission, then the small species can use the pathogen to drive the larger species extinct; small species are abundant and recover quickly from outbreaks, while rarer large species cannot recover from frequent epidemics. Ultimately, only the smallest species survive, and they revert to the epidemic behavior they exhibited when between-species transmission was rare.

This exercise suggests that understanding rates of between-species transmission is an additional, vital component of disease dynamics. To that end, Who Acquires Infection From Whom (WAIFW) matrices provide a framework to examine how the pathogen moves between different groups of hosts and allows us to identify which section of the population acts as a reservoir to maintain the infection and which are subject to spillover events. The matrices were originally developed to study the transmission of pathogens such as measles between different age classes in human populations.<sup>10,11</sup> They were crucial in understanding how HIV moved between different sections of the population during the AIDS epidemic<sup>12</sup>, and they will be central to understanding the efficacy of the social distancing now being put in place for the COVID-19 epidemic.

These matrices are informing the social distancing guidelines now being put in place for the COVID-19 epidemic. Essentially, we are trying to massively reduce the strength of interactions across all age classes and completely remove the interactions between young and old in order to protect people who seem to be more susceptible once infected. Quantifying the structure of these transmission matrices is crucial for understanding the size of the epidemic and how to control its spread.

*Read the extended text [here](#).*

## REFERENCES

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