Disease control framework based on spatial epidemiology: Reply to comments on “Pattern transitions in spatial epidemics: Mechanisms and emergent properties”

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Before delving into the details of the commentaries on review [1], we would like to express our gratitude to all the commentators for sharing their valuable insights. These insights are very much in line with our original intention for review [1], i.e., enticing the discussion on pattern transitions and the implications thereof for spatial epidemiology. Such a discussion is necessary because the work in this particular research field is far from over. There are many opportunities for further discoveries and breakthroughs among which some of the more promising are emphasized in the following.

Past two decades witnessed the disruptive power of several emerging or re-emerging diseases (EIDs) that imperil public health in a manner fundamentally different from sustained diseases (SDs) [26]. While the latter were the main topic of review [1], it is the former that are receiving increasing intention in the literature. It is thus not surprising that the spectrum of modeling tools

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to capture the spatial dynamics of EIDs has exploded above and beyond the stylized mathematical approaches on which we put emphasis, i.e., reaction-diffusion equations and cellular automata. With the rapid development of modern infrastructure [3], it is particularly important that a disease can spread in distant “jumps”, thus requiring a mathematical description in terms alternative to diffusion because assuming a diffusive process implies movement by means of local, Brownian-type jumps. A generalization of Brownian-type jumps would be Lévy flights that, in sharp contrast with the diffusion process, allow the disease to in principle jump any distance. Despite being very different from Brownian motion, Lévy flights are still conducive of pattern formation [4], suggesting that some of the central tenets stressed in review [1] still play key roles. For example, if patterns do form, then their transitions can make a critical difference as an early warning indicator of an outbreak. Having a successful early warning system in place may alleviate much damage associated with infectious diseases and improve the quality of life of the general population.

Mathematical models are an extraordinarily convenient instrument for revealing the transmission dynamics of infectious diseases. Especially so if the temporal dimension of the problem is appended with spatial dimensions. However, even the models of spatial epidemiology are not absolutely honest representations of complex reality. So far, for example, going beyond a single disease transmitted through a single pathway has been relatively rare in epidemiological research. Refs. [5] and [6] thus rightly point to the possibility that several strains of a disease can coexist in the same population and can be transmitted through multiple channels. To expand the reach of epidemiological studies and tackle the mentioned situations, theoretical modeling may need help from new techniques. Two such techniques are agent based models (ABM) and multi-agent systems (MAS) [6]. ABMs in particular have the potential to explain how pathogen diversity interacts with spatial heterogeneity (e.g., population structure and movement) to form new patterns and to trigger transitions between these patterns. Immunity may play an important, and tricky, role as a factor in population structure heterogeneity. In the case of malaria, a large part of population in a high transmission setting usually develops immunity that prevents the symptoms from surfacing, yet fails to completely eliminate the malaria parasite. As a consequence, this “immune” population serves as a reservoir for malaria to resurface after the next rainy season [7].

A spatial pattern describes the spread of diseases in terms of the current state. A pattern transition, by contrast, pertains to the future development of diseases. If a disease is, for instance, analyzed using an SIRS model, target and spiral waves [8–10] are two frequently observed patterns. The transition between target and spiral waves suggests a change in the prevalence of the disease, thus pointing to a possible link between the theoretical model results and clinical studies. Of course, transitions between other types of patterns also exist. Ref. [11] referred to a transition

from stationary patterns to patch invasion. The term “patch invasion” indicates that the disease is distributed in isolated patches from which there is only a low probability of outbreak. Consequently, finding and implementing public health measures that would induce this kind of transition is an interesting problem for future epidemiological research.

Our list of key factors influencing pattern transitions included spatial heterogeneity, seasonality and noise, and human behavior, yet this may not be exhaustive. Liu [12] argued that time delay can also be a crucial factor for the pattern transitions of infectious diseases. On the one hand, time delay increases the risk of extinction for the disease. On the other hand, time delay implies that the disease is poorly controlled and hence difficult to eliminate. Further focus is therefore warranted on the role of time delays in driving the disease spread. Wu [13] furthermore pointed out that climate change may exert an important influence on pattern transitions. Climate change is one of the most pressing global issues associated with modernization. Negative effects of climate change on biological systems have been documented extensively, including biodiversity loss, biological invasions, and ecosystem collapses. At the same time, climate is known to modulate the incidence of some diseases [14]. Having a potential to bring about far-reaching disruptions, the impacts of climate change on diseases dynamics require systematic research in the context of prevention and control of infectious diseases.

An important remark is made in Ref. [15] that public health measures should aim at eliminating familiar patterns caused by spreading diseases. Although somewhat unappealing to researchers focused on elucidating pattern formation and transitions, this perspective is in line with a previously mentioned idea of triggering transitions from stationary patterns to patch invasion. Pattern elimination may therefore guide the development of mathematical studies in the realm of public health actions, especially for infectious diseases that strongly interact with the environment. Ref. [15] further indicated that complexity stems from very basic interactions, proposed by Prigogine in the theory of self-organization based on non-equilibrium thermodynamics. While our failure to mention Prigogine is inexcusable, several of the co-authors of review [1] devote considerable attention to understanding such basic interactions. It is precisely for this reason that we focus on epidemiology in complex networks [16] and emphasize the role of such basic mechanistic principles as (i) connecting individuals in time-evolving networks, (ii) allowing each individual to be in one of several states, and (iii) letting individuals cause their immediate neighbors to switch states. Time-evolving networks with properties (i)-(iii) exhibit extremely rich dynamics, including spontaneous transitions between the phases of high and low activity [17–19]. This transitioning behavior is important because it indicates the potential for a contagion to abruptly spread through a large part of susceptible population. Finally, to set the record straight, we do wish to mention

that Alan Turing was the first to reveal how stationary patterns emerge from reaction-diffusion equations in his now seminal paper [20].

Human behavior is a key factor affecting the spread of diseases [21]. Individual mobility is one important aspect here. Nowadays the global air transportation network allows people to travel between almost any two points on Earth within one day. In line with the previous remarks on EIDs and Lévy flights, the global air transportation network is an example of a science and technology system that simultaneously improves our lives and brings about new dangers with which humanity needs to learn how to cope [22]. In a similar context, Ref. [23] emphasizes the influence of cities on the spread of diseases, once again bringing us to the need to account for distant jumps in the dynamics of disease transmission—an issue for which complex networks represent a natural modeling framework [24].

The long sought after goal of spatial epidemiology are the most effective control measures, yet this goal remains elusive, especially the control measures based on pattern transitions. It is in humanity’s best interest therefore to keep working on the models of infectious diseases thereby incorporating into these models an ever increasing number of factors relevant to the disease dynamics. A likely venue for progress is coupling theoretical models with realistic data following the “big data” paradigm [25,26]. A consequence of such coupling may lead to considerable improvements in public health policies over the coming decades. In the described grand scheme of things, it is safe to say that mathematical models should remain one of the most promising tools for the foreseeable future.

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