# *A complex system perspective on the emergence and spread of infectious diseases: integrating economic and ecological aspects*

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## Abstract

The emergence and spread of infectious diseases reflects the interaction of ecological and economic factors within an adaptive complex system. We review studies that address the role of economic factors in the emergence and spread of infectious diseases and identify three broad themes. First, the process of macro-economic growth leads to environmental encroaching, which is related to the emergence of infectious diseases. Second, there are a number of mutually reinforcing processes associated with the emergence/spread of infectious diseases. For example, the emergence and spread of infectious diseases can cause significant economic damages, which in turn may create the conditions for further disease spread. Also, the existence of a mutually reinforcing relationship between global trade and macroeconomic growth amplifies the emergence/spread of infectious diseases. Third, microeconomic approaches to infectious disease point to the adaptivity of human behavior, which simultaneously shapes the course of epidemics and responds to it. Most of the applied research has been focused on the first two aspects, and to a lesser extent on the third aspect. With respect to the latter, there is a lack of empirical research aimed at characterizing the behavioral component following a disease outbreak. Future research should seek to fill this gap and develop hierarchical econometric models capable of integrating both macro and micro-economic processes into disease ecology.



## Keywords

Adaptive complex systems; hierarchy theory; infectious diseases; environmental encroaching; adaptive human behavior; motivational crowding-out.

## 1 Introduction

The emergence and spread of infectious diseases is determined by the interaction of both ecological and economic factors, while disease ecology openly recognises how the natural environment and the socio-economic system form an adaptive complex system (Pearce & Meletti, 2006; Diez Roux, 2007). As noted by Prigogine (1978) adaptive complex systems are hierarchical systems operating on different levels, corresponding to different spatio-temporal scales, that change their identity in time. Referring to hierarchy theory (Allen & Starr, 1988), when analysing the dynamics of infectious diseases, is important for at least two reasons. First, it immediately allows one to accept how such phenomena have multiple identities (e.g., social, ecological, economic). Whyte *et al*. (1969) write "a system is hierarchical when alternative methods of description exist for the same system". Second, it allows one to better understand how both the emergence and the spread of infectious diseases reflect the interactions of processes occurring at different spatio-temporal scales. As we will discuss later, this is particularly important in epidemiological phenomena where, for example, on a lower level individual behaviour may shape the course of an infection and at the same time be affected by it (i.e., human behaviour is adaptive) while on a higher level, macroeconomic expansion and environmental encroaching may favour the emergence of new diseases.

Comment [g1]: Reviewer 2

The aim of this article is to provide a narrative of the economics and ecology of infectious diseases from the perspective of adaptive complex systems and define a framework of analysis for future research. Given the nature of the task, the literature survey cannot be comprehensive.

By adopting a complex system perspective we try to better motivate the necessity of integrating economics and disease ecology and to clarify how economics together with other social sciences may contribute to achieve a better understanding of disease emergence and spread.

The remainder of the paper is organized as follows. In the second section we shortly introduce the theory of adaptive complex systems and report one important lesson, namely that causes in complex systems may emerge at different hierarchical levels at the same time. This broad ecological perspective is subsequently developed to address the specific problem of emergence/spread of infectious diseases, by calling for a comprehensive analysis spanning across different spatio-temporal scales. In the third section we look at how causality operates at "intermediate levels" and emphasize the role of autocatalytic loops and negative feedbacks operating at such scales. These processes are illustrated by referring to the existing literature on the role of globalization in disease emergence/spread, the economic impact of diseases, and the health policy responses. In the fourth section we discuss how causality can proceed from "upper levels" in the hierarchy and succinctly summarize the interactions between the "macro" processes of economic growth, environmental degradation and disease emergence. In the fifth section, we illustrate how causality can act from "lower levels" in the hierarchy and discuss the role of "micro" processes, with particular attention to the adaptivity of human behaviour. We believe that it is in this area that economics may provide a decisive contribution. However, we also maintain that in order to do so, economists must be willing to go beyond the existing paradigm and embrace insights from other social sciences, including psychology. In the sixth section we attempt to develop a framework for future research in this direction. We point out how efforts should be devoted to the construction of hierarchical econometric models capable of

**Comment [g2]:** Rev 2 suggests to provide an early definition of autocatalysis

integrating both macro and micro-economic processes into disease ecology. In the last section we present some concluding remarks.

## 2 The ecology of infectious diseases and the theory of adaptive complex systems

Comment [g3]: The language in this section mainly refers to ecological processes rather than epidemiological ones. If this is intentional a clearer connection with diseases must be made.

Because infectious diseases originate from the interaction of both ecological and socio-economic processes in an adaptive complex system, the integration of multiple perspectives, specifically socio-economic and ecological is not only useful but necessary (Wilkinson *et al*., 2011). Until now, empirical research on the economics of infectious diseases has mainly focused on the assessment of their monetary costs (Daszak *et al*., 2000; Pimentel *et al*., 2005; Chou *et al*., 2004).This is certainly an important contribution, since disease control has to rely on limited financial resources. On a more abstract level, there is also an abundant literature on the optimal management of infectious diseases (see Ceddia 2012 for a recent contribution, which also surveys the relevant literature). There is no doubt, however, that economics is capable of providing additional contributions to the understanding of both the emergence and the spread of infectious diseases.

Hierarchy theory provides a starting point to understand the connections between the economics and the ecology of infectious diseases. Through these lenses epidemiological phenomena can be seen as the result of processes that occur at different spatio-temporal scales forming nested levels in the hierarchy. For our purposes, and drawing on Ulanowicz (1997), we can define:

1. The focal level: this is the level at which the analyst chooses to map the phenomena of interest (i.e., the emergence/spread of infectious diseases). In the present context we associate it with the socio-economic system, intended as the collection of individuals and

institutions, which are responsible for the various socio-economic processes and it can be defined at an international, national or regional level (depending on the scale of the analysis). This is the scale at which the processes of macroeconomic growth, globalization , infectious disease spread and control policies can be mapped.

2. An upper level: this is the level immediately above the focal one. We associate it with the biophysical context (e.g., the entire biosphere or a particular ecosystem, depending on the scale of the analysis) within which the socio-economic system is ultimately embedded. The upper level reflects the global or macro-regional scale where changes in ecosystem processes and structures can be analysed. This is the scale at which, for example, anthropogenic climate change or global environmental change can be mapped.
3. A lower level: this is the level immediately below the focal one. We associate it with the 'micro' units that compose the socio-economic system. This is the scale at which, for example, individual human behaviour (e.g., pattern of social contacts) can be mapped[1].

Ulanowicz (1997 and 2009) notes how in complex systems causation can emerge at different hierarchical levels simultaneously. This represents a significant departure from the traditional

[1] The identification of the hierarchical structure, intended as the set of processes belonging to the different levels, reflects the choice of the analyst with respect to the phenomena described and the purpose of the analysis. This is explicitly stated by Rosen (1977, p. 29), who claims "a complex system is one which allows us to discern many subsystems depending entirely on how we choose to interact with the system". Our choice to consider the socio-economic system as a sub-part of the larger biophysical context (e.g., the biosphere) has two reasons. First, it is in line with the ecological-economic paradigm (e.g., Daly, 1991). Second, it allows us to provide a narrative about the emergence of infectious diseases consistent with that paradigm, by referring to the idea of environmental encroaching (as discussed in section 4 of the manuscript).

approach, which ascribes causality to one single level. The lower level normally provides the "mechanical" explanation for the events occurring at the focal level. The vast literature on microbial evolution/adaptation (not discussed in this article) and the emergence/spread of infectious diseases is emblematic in this respect. One aspect that we do discuss in section six, is the role of human behaviour in shaping the course of an epidemics. The analysis of human behaviour (albeit in a particular context) constitutes the core of economics. At the same time although the importance of behaviour in disease spread is openly recognised, empirical research in the area is still sparse (Fergusson, 2007). Causality from the upper level normally expresses itself in the form of constraints on the focal level dynamics . As we discuss in section four, the emergence of infectious diseases is indeed related to the expansion of the macro-economy and the consequent environmental degradation. At the focal level, causation is reflected in the presence of autocatalysis. An autocatalytic loop defines an interaction of two or more processes that are mutually reinforcing. As we discuss in section three, macroeconomic growth and globalization constitute a positive feedback in the context of the emergence/spread of infectious diseases. Another example is given by the mutually reinforcing relationship between disease and poverty. However, not all the interactions occurring at the focal level are autocatalytic, as negative feedbacks are also important. For example, in response to the increasing threat of pandemic diseases international health regulations have become more stringent.

To sum up, complex system theory suggests that in order to properly understand the emergence and spread of infectious diseases it is important to analyse a set of relevant processes that span across different spatio-temporal scales, as defined by the focal, upper and lower levels. This task, as we will argue in the course of this article, can only be accomplished by using integrated/multidisciplinary approaches.

**Comment [g4]:** This point needs to be clarified later. The main way in which upper levels cause things to happen in the lower levels is by setting constraints.

**Comment [g5]:** Define autocatalysis

## 3 Causality within the focal level: autocatalytic loops and negative feedbacks

When considering infectious diseases dynamics, important causal elements can be found at the focal level. At this level, the identification of causality is related to the emergence of autocatalytic loops. At the same time it is important to recognise how not all the interactions at this level are autocatalytic as others, equally important, may be characterized by negative feedbacks. The focal level in the present context is associated with the socio-economic system. Among the numerous set of interactions occurring at this level, we will discuss three that appear to be particularly suited to illustrate the operation of causality. Two of such interactions, namely the relationship between macroeconomic growth and globalization and between disease prevalence and macroeconomic growth, point to the existence of autocatalysis. The third one, the relationship between disease prevalence or risk and health policies, indicates the existence of a a self-stabilizing process.

**Comment [g6]:** Rev 2: autocatalysis should be defined earlier

**Comment [g7]:** Rev 2: rephrase "A third relationship…"

### *3.1 Macroeconomic expansion, globalization and infectious diseases*

Economic theory points out how the relationship between the level of economic activity (for example as indicated by the Gross Domestic Product) and the volume of trade tends to be a reinforcing one: more open economies tend to grow faster and larger economies trade more (e.g., Baltagi *et al*., 2003). Although the process of economic globalization has been occurring for centuries (Borghesi & Vercelli, 2004), it has accelerated recently with trade liberalization and fossil fuel transport technologies and it has been accompanied by an unprecedented

macroeconomic growth[2]. If macroeconomic expansion plays a role in the emergence of infectious diseases (as we will discuss in the following section), then the autocatalytic process just described can only amplify the problem. Globalization affects the ecology of pests and pathogens by providing them with new access routes to previously uncolonized areas and by increasing the degree of connectivity between potential disease nodes (e.g., Perrings *et al.*, 2010), as the recent case of SARS illustrates (Peiris *et al.*, 2003).

*3.2 The macroeconomic cost of infectious diseases*

Another set of self-reinforcing processes within the focal level refers to the interactions between socio-economic conditions and disease emergence/spread. There is no doubt that the emergence/spread of infectious diseases can have large socio-economic implications, as the HIV epidemic in Africa shows us (Haacker, 2004). Accounting for the macro-economic costs of infectious diseases has been an important focus of economic analysis as applied to epidemiological phenomena. Aside from the case of HIV in Africa, examples of epidemics accounting include the works of Chou *et al.* (2004), estimating the total macroeconomic impact of the 2003 SARS at US$30-100 billion; Barber *et al.* (2005) estimating the cost of a single outbreak of West Nile Virus in Sacramento County at US $ 2.98 million; Daszak *et al.* (2000) reporting an economic burden of Lyme disease treatment in the USA of US $ 500 million per annum; Pimentel *et al.* (2005), reporting the cost of crops, livestock and human exotic pathogens in the USA as high as US $ 120 billion per annum; Pimentel (2005) estimating the direct costs of

**Comment [g8]:** The previous statement was unsupported.

**Comment [g9]:** Rev 2: confusion about which processes belong to which level and/or to interactions between levels. This needs clarification. I think the general analysis is focused on the "focal" level. The things that matter either happen in this level or in different levels but are related to the focal. Clearly this all depends on the eye of the investigator.

**Comment [g10]:** Perhaps it would be useful to distinguish between emergence (i.e., new disease) and establishment (of an existing disease).

[2] For example, World Bank data show that over the period 1970-2009 world trade has increased from 28% to almost 50% of the global GDP. During the same time, the global GDP valued at constant 2000 US $ passed from over 12 trillion to over 41 trillion.

pesticide application in USA at approximately US $ 10 billion per annum, to which indirect costs (e.g., environmental, health related etc.) of about US $ 9-12 billion per annum must be added. At the same time it is well understood that poor socio-economic conditions may favour both the emergence and the spread of several infectious diseases. Infection emergence/spread and poor socio-economic conditions also form an autocatalysis.

*3.3 Infectious diseases and health policies*

Not all interactions at the focal level are self-reinforcing. The emergence/spread of infectious diseases, for example is likely to trigger policy responses at both the national and international level. A good example, in this respect, is provided by the recent changes to the International Health Regulations (IHR) of the World Health Organizations. As noted by Dry (2008), when they were first introduced in 1969 IHR mainly aimed at preventing a disease crossing the national borders. In a globalized age clearly such an effort is likely to be vain unless a global surveillance network is established. Hence, in response to an increased threat of pandemic diseases, in 2005 the IHR were modified and put a stronger emphasis on the role of surveillance. If effective, such policies will slow down the spread of the disease revealing a negative feedback between disease risk and policy responses, which resemble those operating in a prey/predator system. Other negative feedbacks at the focal level may result, for example, by the effect of health policies restricting global travel and/or trade (e.g., the trade restrictions following the 2001 UK Foot and Mouth epidemic).

**Comment [g11]:** And establishment?

## 4 Causality from above: macroeconomic scale, environmental degradation, and the emergence of infectious diseases

When looking at the ecology of infectious diseases, causality can proceed from the upper level. Causality from above is normally expressed in the form of constraints on the dynamics of the phenomena occurring at the focal level (Ulanowicz, 1997). Empirical evidence supports this hypothesis. One of the causes behind the emergence of infectious diseases is the encroaching of a growing socio-economic system (the focal level) into a finite biosphere (the upper level). This can be interpreted as the manifestation of a biophysical constraint (alongside many other signs of environmental stress) on macroeconomic growth. Human activities at the macro level play an important role in the emergence of infectious diseases either directly or indirectly by causing ecological changes (e.g., anthropogenic climate change). Macro socio-economic factors have been shown to be important explanatory variables for the emergence of the majority of infectious diseases over the past 60 years (Jones *et al.*, 2008). On one hand, the expansion of the human/economic system within the finite biosphere leads to encroaching into previously pristine areas with consequent exposure to a pool of known and unknown pathogens (Daszak *et al.*, 2001; Wilson, 2001; Price-Smith, 2002). For example, changes in farming practices and habitat destruction may have played a role in the emergence of the Nipah virus, transmitted from bats to pigs and then to humans (Chua et al., 2000). The spread of livestock factory farming (as opposed to more extensive practices) is associated with outbreaks of *E. coli* O157:H7 in Canada (Ali, 2004). Similar phenomena might have played an important role in the emergence of Ebola, HIV/AIDS and Marburg viruses (Daszak *et al*., 2000). Moreover economic expansion is often accompanied by a series of socio-economic changes, including population ageing, which can also play an important role in increasing population susceptibility . Finally environmental change

resulting from macroeconomic growth can also lead to the emergence of infectious diseases. Anthropogenic climate change, for example, is likely to have important effects on both the distribution and the incidence of various diseases, including malaria, dengue and viral encephalitides (Patz *et al*., 1996).

**Comment [g12]:** Rev 2: what about globalization and re-emergence of TB in developed countries or SARS spread?

## 5 Causality from below: individual behaviour and infectious diseases

At the lower level, the search for causes is normally intended as the identification of the "mechanisms" that lead to the emergence of the phenomena observed at the focal level. The vast literature on the role of microbial adaptation well exemplifies the attempt to understand the mechanisms behind the emergence/spread of infectious diseases. Rather than reporting the existing literature on microbial adaptation, we will focus on one aspect that is (in our opinion) equally important and more amenable to treatment by economists: individual behaviour. At the micro level, economics can play an important role in understanding disease ecology because it is concerned with the choices of economic agents. According to economic theory such choices refer to the rational allocation of economic resources in order to maximise an individual's well being or profit. In both cases economic theory has developed analytical tools that allow researchers to model the process of decision making of rational agents and consequently explain their behaviour. Moreover, advances in economic theory point towards novel approaches to modelling human behaviour which, going beyond the traditional *Homo Oeconomicus*, are increasing the realism of psychological underpinning in economic analysis and generating theoretical insights on the basis of empirical research (Camerer and Loewenstein, 2004). The

**Comment [g13]:** Switch to disease ecology?

application of psychological concepts within economic models is opening up new avenues of research in several domains and thus also in the economics of infectious diseases.

*5.1 Adaptive human behaviour*

McCallum *et al*. (2001) identify three factors which determine the rate at which new infections occur in a given population: the contact rate, the proportion of contacts with susceptible individuals and the probability that once an 'appropriate' contact has occurred, the infection will be transmitted. If the contact rate between individuals is (at least partially) determined by probability judgments and behavioural choices, then cross fertilization between economics and psychology can provide useful insights. The recognition that an individual's behaviour should be explicitly included in models of epidemics is not new. A more interesting observation is that, at least for directly transmitted diseases, human behaviour is likely to be adaptive as it will at the same time affect and respond to the course of epidemics. Unfortunately to this date empirical research, which explicitly matches adaptive behaviour to epidemics, is sparse (Fergusson, 2007). In the case of HIV/AIDS, where the trade-off between engaging in desirable activities (e.g., frequently changing sexual partners) and the associated risk of contracting the disease is particularly stark, evidence indicates how behavioural changes have occurred with the progression of the disease prevalence (Becker and Joseph, 1988). Similarly, during the 2003 SARS epidemics in Hong-Kong individuals showed increased attitude to reducing social contacts as the epidemics progressed (Lau *et al*., 2005).

Although human behaviour is so important in the spread of a disease, and individuals alter their behaviour when the disease progresses (as in this case also the probability of getting infected will change), it is common to model behaviour as independent from prevalence, with empirical

efforts to characterise the contact rates by relying on time use survey data (Zaghegni *et al*., 2008) and/or population surveys (Mossong *et al*., 2008). Alternatively, the assumption is made that contact rates are decreasing with respect to infection prevalence (D'Onofrio and Manfredi, 2009; McCallum *et al*., 2001). These approaches, despite attempting to control for human adaptation, are either static or impose an exogenous relationship between disease progression and human responses. Such limits are recognised by disease ecological-economic models, where individuals are assumed to make choices in order to maximise their expected utility (e.g., Reluga, 2010; Fenichel *et al*., 2011). Disease risk is endogenous, as it is both determined by and determines individual choices, revealing a feedback between the infection prevalence and human behaviour which in turn shapes the spread of disease. To this date such ecological-economic models have been mainly developed on a theoretical basis in order to perform numerical simulations (e.g., Fenichel *et al.*, 2011). However, the possibility of conducting experiments to explain inter-temporal risky choices (Frederick *et al*., 2004) may provide an empirical basis to capture the role of adaptive human behaviour in the spread of infectious diseases. An alternative strategy might be to track individual behaviour by using diaries/journals (Beutels *et al*., 2006).

**Comment [g14]:** Disease ecological-economic models?

*5.2 Beyond Homo Oeconomicus*

Economic theory suggests that human behavior can largely be understood as individual rational action, in a particular sense. This means that actions are the result of people's preferences and beliefs. The former are generally taken as given and to include all aspects of people's motivational states, including their desires, goals, values and so on. The latter are usually taken to be well-informed beliefs, although there are branches of economics such as asymmetric information and bounded rationality theories which relax this assumption. Economists have also

analysed cases where individually rational and socially desirable actions diverge. A central case of relevance to this article is that of “public goods”, defined as goods which are non-rival and non-excludable. These properties imply that it is problematic to supply public goods through markets, because of the free-rider problem.

Infectious disease control has public good properties since, for whatever level of disease control attained, everyone benefits regardless of whether they help meet the costs involved. These costs are not only financial. For example, a vaccination program for swine flu might involve each participant suffering a mild version of the symptoms of the pathogen, but the public health benefits of this action (a small increment in 'herd immunity') accrue to the entire population. Although there are private benefits from vaccination (self-protection), a person for whom self protection is outweighed by the induced symptoms would not be expected to be swayed by the public health rationale for vaccination. Moreover, an individual who has been infected may have no rational choice reason at all to avoid infecting others, since he or she would incur the costs of self-isolation, would not benefit from disease control, and might not feel sufficiently altruistic towards the generality of the rest of the population to pay those costs.

Economics cannot fully explain the motivational aspect of public health campaigns, since silence on this matter is a corollary of taking preferences as given. In such situations economists (typically) suggest that the best way to change behavior is to alter the “external” incentive structure of the situation, for example by introducing regulations backed by legal sanctions, or personal rewards for the desired actions.

Psychology, on the other hand clearly recognises that human behaviour and preferences are affected by factors normally overlooked by economics. For example, it is well known that in many situations people emulate the behaviour of others. Social pressure can exert a substantial

influence especially when individuals have to take decisions in ambiguous or critical situations (Cialdini, 1993).

Another important insight from psychology relates to the interactions between extrinsic and intrinsic motivations and its implications for appropriate policy design. People are motivated to do the right thing not only because of extrinsic motivations, but also for intrinsic rewards. Extrinsic motivations refer to the set of incentives applied from outside and include both economic incentives (e.g., changes in relative prices through taxes/subsidies) and regulatory ones. Intrinsic motivations come from within the person (Deci, 1971). Although economists do not deny the existence of intrinsic motivations, they normally assume that they can just be added to extrinsic ones. Hence, introducing economic incentives will always generate the desired behavioural changes. In the context of the consumer choice theory, for example, it is assumed that changes in income and/or relative prices (i.e., the extrinsic motivations) will not affect the shape of the preference maps (i.e., the intrinsic motivations which are taken as given). Empirical results show how this is not always the case (Frey and Oberholzer-Gee, 1997; Bowles 2008). This apparent paradox is explained through the motivational crowding-out effect. The introduction of extrinsic motivations may in some cases lead to the weakening of intrinsic motivations to such an extent that the total effect is a behavioural change in an undesirable direction. For instance, in comparing voluntary and paid blood donation, supplies were more forthcoming under the former regime, and the blood was also of higher quality (Titmuss, 1970). Thus economic incentives triggered a crowding-out effect which, repressing the expression of altruism on behalf of donors, created counterproductive effects in the “blood market”.

These considerations are likely to be important in the context of infectious diseases. As the role of human behaviour in the spread and emergence of infectious diseases becomes more apparent,

policy interventions aiming at promoting desired behavioural changes (e.g., social distancing) may be required. It is then crucial to understand how such policies will affect aspects influencing adaptive behaviour (social norms, habits, choices involving computations and intrinsic motivations) in order to avoid counterproductive results.

## 6 Directions for future research

In the previous sections, drawing on adaptive complex systems and hierarchy theory, we have attempted to provide a narrative integrating the economics and ecology of infectious diseases. The main lesson from complex systems theory is that causality can operate simultaneously at different hierarchical levels. It is worth dwelling for a moment on this, by identifying three broad themes. First, causality from the upper level normally manifests itself as a constraint on the focal level dynamics. We have discussed how the process of macro-economic growth within a finite biosphere leads to environmental encroaching, which in turn is related to the emergence of infectious diseases. The case of the Nipah virus provides a fitting example, where deforestation and bats habitat destruction has favoured the transmission of the virus first to pigs and then to humans. Second, at the focal level causality manifests itself mainly through autocatalytic processes. The emergence and spread of infectious diseases can inflict significant economic damages, a fact which in turn may provide favourable conditions for the further spread of diseases. The nexus between HIV and poverty in Africa illustrates this point. Similarly, the existence of a mutually reinforcing relationship between global trade and macro-economic growth amplifies the emergence/spread of infectious diseases. Third, causality from the lower level provides the "mechanical" explanation of the focal level dynamics. The role of patterns of social contacts in disease spread is well understood. However, it is also important to

acknowledge how the dynamics at the focal level can also feed-back into lower level processes. Microeconomic approaches to infectious disease management point to the adaptivity of human behaviour, which at the same time shapes the course of epidemics and responds to it. The documented reduction of social contacts during the SARS epidemics in Hong Kong is just one example of the adaptivity of human behaviour in response to disease outbreaks. Our synthesis shows that currently most of the applied research has been focused on the first two aspects, and to a lesser extent on the third aspect. With respect to the latter, there is still a lack of empirical research aimed at characterizing the evolution of contact rates in large populations following a disease outbreak. For the purpose of future research, these considerations have several important implications.

Consider for example the case of an infection occurring in a given population whose size is constant and normalized to 1. Assuming that no immunity exists, at any point in time t, the population can be partitioned into infected/infectious ($I_t$) and susceptible ($S_t=1-I_t$). Let the focal level be the socio-economic system in which the disease occurs, then in this simplified context the system dynamics can be summarised by the equation describing the evolution of the infected class

$$I_{t+1} - I_t = \eta(\cdot)(1 - I_t)I_t - \omega(\cdot)I_t \quad (1)$$

Expression (1) is a good starting point for our discussion since it closely resembles a conventional disease ecology model. This simple model states that the rate of change in infection prevalence depends on the transmission rate ($\eta$) between susceptible ($1-I_t$) and infected ($I_t$)

**Comment [g15]:** Rev 2

**Comment [g16]:** Rev 2 thinks equations 1-3 are redundant, given the well written text.

individuals in the population and on the infection rate of 'decay' ($\omega$). Clearly both the transmission rate and the decay rate are not necessarily constant over time, and given our discussion so far they are affected by changes in environmental conditions ($E_t$), but also by changes in individual behavior ($C_t$), infection prevalence ($I_t$) (since individual behavior is adaptive), macroeconomic factors like trade volume ($T_t$) and GDP ($Y_t$), and by the implementation of specific policies to control the disease ($R_t$). In light of this, expression (1) can be rewritten as

$$I_{t+1} = f_1(I_t, E_t, C_t, T_t, Y_t, R_t) \quad (2.a)$$

Expression (2.a) is interesting for two reasons. First, it can be easily linked with traditional difference-equations models used in disease ecology. Secondly, it provides a natural way to make explicit reference to the connections between processes occurring at all the hierarchical levels.

Consider first the dynamics within the focal level. The arguments presented in the previous sections should persuade us that (2.a) only provides a partial description. A more complete account should also consider the following expressions

$$R_{t+1} = f_2(R_t, E_t, I_t, X_t) \quad (2.b)$$

$$Y_{t+1} = f_3(Y_t, I_t, R_t, E_t, T_t, X_t) \quad (2.c)$$

$$T_{t+1} = f_4(T_t, Y_t, R_t, X_t) \quad (2.d)$$

Expression (2.b) aims at capturing the focal level interactions between changes in health policies ($R_t$) and infection prevalence (as discussed in section three). Clearly, the change in health regulations will also depend on other factors which may include both prevailing environmental conditions ($E_t$) and other explanatory variables that we generally call ($X_t$). Expressions (2.c – 2.d) try to capture the autocatalytic loop between macroeconomic growth and trade, while at the same time they acknowledge the role of infection prevalence ($I_t$), health policies ($R_t$), environmental conditions ($E_t$) and other possible explanatory variables ($X_t$).

Consider now the upper level dynamics. In this respect we strongly encourage continuing on the existing research path that openly acknowledges the role of an expanding macroeconomic system in causing environmental changes that may lead to the emergence of infectious diseases (Daszak *et al.*, 2001; Price-Smith, 2002). Formally this can be expressed by the need to characterise the following relationship

$$E_{t+1} = f_5(E_t, Y_t, X_t) \quad (3)$$

Expression (3), which synthesizes the arguments presented in section four, posits that the change in the prevailing environmental conditions ($E_t$) will depend on the macroeconomic scale of the socio-economic system ($Y_t$) plus other explanatory variables (e.g., socio-demographic indicators) ($X_t$).

Consider next the lower level dynamics. We have identified the need to achieve a better integration of micro-economics and epidemiology by explicitly incorporating human behaviour into infectious disease models and recognising that such behaviour is adaptive (i.e., there is a

feedback between the state of the epidemiological phenomena and human behaviour). Although attempts to incorporate behaviour have been made (e.g., the use of time use survey data suggested by Zaghegni *et al.*, 2008 and the characterization of mixing patterns by Mossong *et al.*, 2008) the existing approaches fail to capture its dynamic and adaptive component. Given the paucity of existing applied research, we believe that future efforts should concentrate on this aspect, and that is why the remaining part of this section will focus on it. The obvious question then is: what determine changes in the behavioural variables? Answering this question requires a careful assessment of the disease under consideration and the socio-economic and ecological circumstances.

*6.1 Characterizing adaptive human behaviour*

We already discussed how human behavior (e.g., contact rates, that we labeled $C_t$) plays an important role in shaping the course of an infection. As individual behavior is adaptive it will certainly change as the structure of prevailing incentives and pay-offs (here intended as extrinsic motivations) change. First, as the pay-offs reflect the benefit/costs associated with the contact rates, it is likely that the latter will depend on the general macroeconomic conditions ($Y_t$). For example, in the case of zoonotic diseases the ability of an individual to reduce contacts with animals will clearly depend on its effects on economic returns and so on factors like economic damage, market prices, costs of equipment, type of farm, economic status and level of education. The willingness of an individual to avoid travelling and spread and/or contract an infectious disease will depend also on her socio-economic status. Similarly the incentives for an individual to seek treatment will also depend on the set of prevailing incentives. Therefore, for a given disease and relevant populations, data on socio-economic characteristics need to be considered.

As the pay-offs are likely to be different for infected/infectious and susceptible individuals (and as the proportions of each in the population change with changes in prevalence), the behavioural variables will change with infection prevalence. The very fact that human behaviour is adaptive indicates that it is dynamic and responsive to changes in the infection prevalence. The main challenge in the future will be to collect data on person-to-person and person-to-animal contact rates over a relevant period of time following an outbreak and try to understand how the contact pattern responds to the infection progression. This could be done using ethnographic approaches and/or diaries and surveys (Beutels *et al*., 2006). Where the evolution of contact rates in a given population at the time when an epidemic develops cannot be readily observed, suitable proxies should be identified. For human infectious diseases for example, such proxies could include data on public transport traffic (e.g., Bharti *et al*., 2008), international travel data (Johansson *et al*., 2011) and/or hours spent watching TV or engaging in other home activities (as opposed to engaging in social activities). These considerations extend to the other relevant behavioural variables (e.g., decision to take medical treatment or vaccination etc.).

Finally, it is essential to recognise how what matters for individual behaviour are the perceived costs/benefits (e.g., Rubin *et al*., 2009). Therefore when accounting for adaptive human behaviour it is important to factor in elements like the novelty of the disease, public perceptions, scientific understanding and in general elements that reflect the amount and quality of information available about the disease prevalence and its consequences.

### *6.2 Characterizing the interactions between intrinsic and extrinsic motivations*

In section five we introduced the distinction between extrinsic and intrinsic motivations as determinants of human behaviour. Efforts to understand the human behaviour components in

disease ecology models should account for both. This may seem an almost impossible task, as unlike extrinsic motivations (e.g., regulations and/or price mechanisms like fines and/or taxes/subsidies) intrinsic motives are difficult to quantify. However, as pointed out by Frey (1997), this is not necessarily a problem as long as one is able to characterize the relationship between intrinsic and extrinsic motives. Both sets of motives (we label intrinsic motives *W* and consider health policy *R* as an example of extrinsic motives) will have an impact on the behavioural variables. Again, for simplicity consider the social contact rate ($C_t$) as an example of behavioural variable. The role of extrinsic and intrinsic motives in shaping this variable can be captured as $\Delta C_t=C_{t+1}-C_t=f(...W_t,R_t...)$. Recent developments in behavioural economics (see Bowles 2008 for further references), show that extrinsic motivations may affect intrinsic ones so that $W_t=h(R_t)$. Consider for example the case in which a local government, in response to an epidemic of swine flu, is planning to introduce some regulations to restrict people's abilities to use public transport and/or to attend crowded places (e.g., bars, clubs etc.). If the introduction of such an extrinsic motivation interacts with the individuals' intrinsic motivations the total effect on individuals' behaviour can be written as

$$\frac{d\Delta C}{dR}=\frac{\partial f}{\partial h}\frac{\partial h}{\partial R}+\frac{\partial f}{\partial R}\lessgtr 0 \qquad (4)$$

We know that $\frac{\partial f}{\partial R}<0$ (as the direct purpose of the regulation is to reduce person-to-person contacts). We also know that $\frac{\partial f}{\partial h}<0$ (as a stronger intrinsic motivation to reduce personal contacts will in general result in a reduction in contacts). Consequently three possibilities arise

a. $\frac{\partial h}{\partial R} = 0$: in this case the total effect will be given just by $\frac{d\Delta C}{dR} = \frac{\partial f}{\partial R} < 0$ and the regulation will have the desired result of restricting personal contacts (this is the normal assumption in mainstream economics)

b. $\frac{\partial h}{\partial R} > 0$: in this case the total effect will be given by $\frac{d\Delta C}{dR} = \frac{\partial f}{\partial h}\frac{\partial h}{\partial R} + \frac{\partial f}{\partial R} < \frac{\partial f}{\partial R} < 0$ and the regulation will be even more effective as extrinsic motivations 'crowd in' intrinsic ones.

c. $\frac{\partial h}{\partial R} < 0$: in this case the total effect will be weaker as extrinsic motivations 'crowd out' intrinsic ones. In extreme cases where $\frac{\partial f}{\partial h}\frac{\partial h}{\partial R} > -\frac{\partial f}{\partial R}$ behaviour may even change in the opposite direction than the intended one.

In some contexts, experimental methods can be used to tease out the sign (rather than the magnitude) of $\frac{\partial h}{\partial R}$ (Bowles, 2008). Such an exercise, to be ideally performed on a case-by-case basis perhaps using localised trials, is necessary for two reasons. First, if a relationship between extrinsic and intrinsic motivation exists in a particular context, one will not be able to properly understand behavioural responses unless that relationship is appropriately characterised. Secondly, any policy proposal aiming at modifying human behaviour for the control of infectious diseases should be designed after considering the possibility of crowding-out effects in order to avoid unpleasant surprises.

The considerations expressed so far suggest that one way to capture the dynamics of the lower level is to characterise the following expression

$$C_{t+1} = f_{\mathfrak{G}}(C_t, I_t, Y_t, R_t, X_t) \quad (5)$$

Expression (5) simply restates that in order to understand the changes in the lower level variables like the pattern of social contacts ($C_t$), its interactions with processes occurring at the focal level, including infection prevalence ($I_t$), macroeconomic conditions ($Y_t$), policy ($R_t$), and other explanatory variables (e.g., disease novelty or information on its consequences) ($X_t$) must be carefully considered.

*6.3 Joint estimation of epidemiological and socio-economic responses*

This last point is a methodological one and relates to the specification of statistical/econometric models required to correctly estimate the relevant parameters in the epidemiological-economic model. It should be clear by now that the ecological and the socio-economic system form an adaptive complex system organized in hierarchical levels, where processes occur at different spatio-temporal scales. Such processes are interdependent and change over time, but possess one over-arching feature which makes them attractive. This feature is that the lower-level entities are each related, but only through the hierarchical nodes stemming from the spatio-temporal chain. The interactions between the processes at a lower level are in this sense an emergent property at the next level of organization. Perhaps the best way to capture these interactions is to use a hierarchical econometric model (Wilke, 2003). The use of hierarchical models per-se in disease ecology is not new (Duncan *et al.*, 1996; Diez Roux, 2000, 2008). As noted by Diez Roux (2000) hierarchical models may be used to explain phenomena at the focal level by accounting also for processes occurring at lower levels, upper levels or both. Despite this plethora of possibilities, in

**Comment [g17]:** This paragraph captures the role of hierarchical approaches. Focal level is the centre and then look at what happens within this level and on the interactions between focal-lower and focal-upper.

epidemiology the models have been chiefly used to explain individual health outcomes by considering upper level variables (e.g., the abundant literature on the social determinants of health). The approach we recommend in this article is novel as it demands to account simultaneously for the role of macro and micro-economic processes, occurring across all three hierarchical levels, in order to explain both the emergence and the spread of infectious diseases. Clearly the detailed development and application of this kind of model is beyond the scope of the current article. Here we would just like to sketch, drawing on the ideas presented so far, how the analyst might proceed in this general direction. At the focal level, expressions (2.a – 2.d) provide an ideal starting point for an econometric model, once error terms are included. Similar considerations can be applied for the characterization of the upper and lower levels dynamics, where expressions (3) and (5) can be considered.

At this stage the reader may feel frustrated, under the impression that our discussion simply posits that everything is related to everything. On the other hand, the traditional analysis of epidemiological phenomena ascribes the causality of emergence and spread clearly to one single level[3]. In general the existing literature is cavalier about the possibility of feedbacks among the various processes both within and between levels (Diez Roux, 2000 and 2008). Our approach, on the other hand, follows from the recognition that in complex systems causality can be found simultaneously at the upper, focal and lower levels (Ulanowicz, 2009). This implies that in order

[3] At the upper level for example, this is reflected in the already mentioned literatures on the social determinants of health and/or on the effect of environmental encroaching. At the lower level, although we emphasized the lack of empirical research accounting for the role of adaptive human behaviour (as noted by Fergusson, 2007), there is a vast literature on the effects of microbial evolution and adaptation (something which may be perceived as a very low level in the hierarchical structure) on the emergence/spread of infectious diseases.

to correctly understand the epidemiological phenomena, the econometric expressions corresponding to (2.a – 2.d), (3) and (5) need to be jointly estimated, where the estimation technique may require the use of simultaneous equations models (e.g., Drezè and Richard, 1983). Failing to do so, will have implications for both parameters estimation and their correct interpretation. However, two considerations are worth making. First, the dynamics associated with the processes occurring at various hierarchical levels are likely to range across different temporal and spatial scales. This is also reflected in the way data are currently collected. For example, data on infection prevalence may be reported on a weekly basis, data on macroeconomic growth may be available on a quarterly basis while some data on changes on individuals contact patterns may be available on a daily basis. At the very least this will require addressing a problem of data harmonization or even to collect new data altogether. Second, as complex adaptive systems change their identity over time, the estimation of the parameters in (2.a – 2.d), (3) and (5) will help to understand the current drivers of change, while our ability to predict will never be complete. We believe that Woolhouse (2011) claim that predictive modelling is "the art of the possible" should be interpreted in this sense.

## 7 Conclusions

In this article we argue that epidemiological phenomena reflect the interaction between ecological and socio-economic processes occurring at different scales forming an adaptive complex system. Perhaps two of the most significant properties of such systems refer to the fact that they are hierarchical systems capable of being described by alternative/multiple perspectives and to the high degree of uncertainty which characterizes their evolution (since they are changing

over time). In this article we have argued for an expansion of the perspectives describing epidemiological phenomena and have suggested possible ways in which the incorporation of economic and perhaps psychological elements into classical disease ecology settings may occur. The uncertainty associated with the dynamics of adaptive complex systems derives from the fact that such systems are always "open" to change. In this sense they are governed not by mechanical laws, but rather by what Popper (1990) would call propensities. Hence even though complex systems tend to follow certain patterns, such patterns can always change. The emergence of new infectious diseases again may help to clarify this point. At a certain time the risk of a pathogen jumping from its animal host to humans may seem negligible (e.g., think about the case of the Nipah virus). Such a conclusion may lead to the widespread adoption of commercial or agricultural practices which in turn make the emergence of the new disease an "accident waiting to happen". When this occurs, the original risk assessment may appear as completely inadequate. One of the reasons for such a failure in prediction may be related to the fact that the analysis ignored the effects of changes in the upper level (e.g., agricultural expansion and deforestation) on both the focal and lower levels. Although the complete elimination of uncertainty in the emergence and spread of infectious diseases may never be achieved, we believe that the use of a multidisciplinary and hierarchical approach, which openly recognises that causality in complex systems may emerge at different levels simultaneously and that accounts for the interactions of ecological and economic processes at different scales, is crucial to improve our understanding of the dynamics of such systems.

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