

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

Article

Accepted Version

Ceddia, G., Bardsley, N., Nocella, G. ORCID: <https://orcid.org/0000-0001-9625-6315>, Goodwin, R., Stasi, A. and Holloway, G. ORCID: <https://orcid.org/0000-0002-2058-4504> (2013) A complex system perspective on the emergence and spread of infectious diseases: integrating economic and ecological aspects. *Ecological Economics*, 90. pp. 124-131. ISSN 0921-8009 doi: <https://doi.org/10.1016/j.ecolecon.2013.03.013> Available at <https://centaur.reading.ac.uk/31937/>

It is advisable to refer to the publisher's version if you intend to cite from the work. See [Guidance on citing](#).

Published version at: <http://dx.doi.org/10.1016/j.ecolecon.2013.03.013>

To link to this article DOI: <http://dx.doi.org/10.1016/j.ecolecon.2013.03.013>

Publisher: Elsevier

All outputs in CentAUR are protected by Intellectual Property Rights law, including copyright law. Copyright and IPR is retained by the creators or other copyright holders. Terms and conditions for use of this material are defined in

the [End User Agreement](#).

www.reading.ac.uk/centaur

CentAUR

Central Archive at the University of Reading

Reading's research outputs online

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

3

4 **1 Introduction**

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

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

Comment [g1]: Reviewer 2

1 By adopting a complex system perspective we try to better motivate the necessity of integrating
2 economics and disease ecology and to clarify how economics together with other social sciences
3 may contribute to achieve a better understanding of disease emergence and spread.
4 The remainder of the paper is organized as follows. In the second section we shortly introduce
5 the theory of adaptive complex systems and report one important lesson, namely that causes in
6 complex systems may emerge at different hierarchical levels at the same time. This broad
7 ecological perspective is subsequently developed to address the specific problem of
8 emergence/spread of infectious diseases, by calling for a comprehensive analysis spanning across
9 different spatio-temporal scales. In the third section we look at how causality operates at
10 “intermediate levels” and emphasize the role of autocatalytic loops and negative feedbacks
11 operating at such scales. These processes are illustrated by referring to the existing literature on
12 the role of globalization in disease emergence/spread, the economic impact of diseases, and the
13 health policy responses. In the fourth section we discuss how causality can proceed from “upper
14 levels” in the hierarchy and succinctly summarize the interactions between the “macro”
15 processes of economic growth, environmental degradation and disease emergence. In the fifth
16 section, we illustrate how causality can act from “lower levels” in the hierarchy and discuss the
17 role of “micro” processes, with particular attention to the adaptivity of human behaviour. We
18 believe that it is in this area that economics may provide a decisive contribution. However, we
19 also maintain that in order to do so, economists must be willing to go beyond the existing
20 paradigm and embrace insights from other social sciences, including psychology. In the sixth
21 section we attempt to develop a framework for future research in this direction. We point out
22 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

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

3

4

5 **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.

6 Because infectious diseases originate from the interaction of both ecological and socio-economic
7 processes in an adaptive complex system, the integration of multiple perspectives, specifically
8 socio-economic and ecological is not only useful but necessary (Wilkinson *et al.*, 2011). Until
9 now, empirical research on the economics of infectious diseases has mainly focused on the
10 assessment of their monetary costs (Daszak *et al.*, 2000; Pimentel *et al.*, 2005; Chou *et al.*,
11 2004). This is certainly an important contribution, since disease control has to rely on limited
12 financial resources. On a more abstract level, there is also an abundant literature on the optimal
13 management of infectious diseases (see Ceddia 2012 for a recent contribution, which also
14 surveys the relevant literature). There is no doubt, however, that economics is capable of
15 providing additional contributions to the understanding of both the emergence and the spread of
16 infectious diseases.

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

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

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

5 2. An upper level: this is the level immediately above the focal one. We associate it with the
6 biophysical context (e.g., the entire biosphere or a particular ecosystem, depending on the
7 scale of the analysis) within which the socio-economic system is ultimately embedded. The
8 upper level reflects the global or macro-regional scale where changes in ecosystem
9 processes and structures can be analysed. This is the scale at which, for example,
10 anthropogenic climate change or global environmental change can be mapped.

11 3. A lower level: this is the level immediately below the focal one. We associate it with the
12 ‘micro’ units that compose the socio-economic system. This is the scale at which, for
13 example, individual human behaviour (e.g., pattern of social contacts) can be mapped¹.

14

15 Ulanowicz (1997 and 2009) notes how in complex systems causation can emerge at different
16 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).

1 approach, which ascribes causality to one single level. The lower level normally provides the
2 “mechanical” explanation for the events occurring at the focal level. The vast literature on
3 microbial evolution/adaptation (not discussed in this article) and the emergence/spread of
4 infectious diseases is emblematic in this respect. One aspect that we do discuss in section six, is
5 the role of human behaviour in shaping the course of an epidemics. The analysis of human
6 behaviour (albeit in a particular context) constitutes the core of economics. At the same time
7 although the importance of behaviour in disease spread is openly recognised, empirical research
8 in the area is still sparse (Fergusson, 2007). Causality from the upper level normally expresses
9 itself in the form of constraints on the focal level dynamics. As we discuss in section four, the
10 emergence of infectious diseases is indeed related to the expansion of the macro-economy and
11 the consequent environmental degradation. At the focal level, causation is reflected in the
12 presence of **autocatalysis**. An autocatalytic loop defines an interaction of two or more processes
13 that are mutually reinforcing. As we discuss in section three, macroeconomic growth and
14 globalization constitute a positive feedback in the context of the emergence/spread of infectious
15 diseases. Another example is given by the mutually reinforcing relationship between disease and
16 poverty. However, not all the interactions occurring at the focal level are autocatalytic, as
17 negative feedbacks are also important. For example, in response to the increasing threat of
18 pandemic diseases international health regulations have become more stringent.
19 To sum up, complex system theory suggests that in order to properly understand the emergence
20 and spread of infectious diseases it is important to analyse a set of relevant processes that span
21 across different spatio-temporal scales, as defined by the focal, upper and lower levels. This task,
22 as we will argue in the course of this article, can only be accomplished by using
23 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

1 **3 Causality within the focal level: autocatalytic loops and negative feedbacks**

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

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

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

13

14 *3.1 Macroeconomic expansion, globalization and infectious diseases*

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

1 macroeconomic growth². If macroeconomic expansion plays a role in the emergence of
2 infectious diseases (as we will discuss in the following section), then the autocatalytic process
3 just described can only amplify the problem. Globalization affects the ecology of pests and
4 pathogens by providing them with new access routes to previously uncolonized areas and by
5 increasing the degree of connectivity between potential disease nodes (e.g., Perrings *et al.*,
6 2010), as the recent case of SARS illustrates (Peiris *et al.*, 2003).

Comment [g8]: The previous statement was unsupported.

8 3.2 *The macroeconomic cost of infectious diseases*

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

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.

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

6

7 *3.3 Infectious diseases and health policies*

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

21

22

Comment [g11]: And establishment?

1 **4 Causality from above: macroeconomic scale, environmental degradation, and the**
2 **emergence of infectious diseases**

3 When looking at the ecology of infectious diseases, causality can proceed from the upper level.
4 Causality from above is normally expressed in the form of constraints on the dynamics of the
5 phenomena occurring at the focal level (Ulanowicz, 1997). Empirical evidence supports this
6 hypothesis. One of the causes behind the emergence of infectious diseases is the encroaching of
7 a growing socio-economic system (the focal level) into a finite biosphere (the upper level). This
8 can be interpreted as the manifestation of a biophysical constraint (alongside many other signs of
9 environmental stress) on macroeconomic growth. Human activities at the macro level play an
10 important role in the emergence of infectious diseases either directly or indirectly by causing
11 ecological changes (e.g., anthropogenic climate change). Macro socio-economic factors have
12 been shown to be important explanatory variables for the emergence of the majority of infectious
13 diseases over the past 60 years (Jones *et al.*, 2008). On one hand, the expansion of the
14 human/economic system within the finite biosphere leads to encroaching into previously pristine
15 areas with consequent exposure to a pool of known and unknown pathogens (Daszak *et al.*,
16 2001; Wilson, 2001; Price-Smith, 2002). For example, changes in farming practices and habitat
17 destruction may have played a role in the emergence of the Nipah virus, transmitted from bats to
18 pigs and then to humans (Chua *et al.*, 2000). The spread of livestock factory farming (as opposed
19 to more extensive practices) is associated with outbreaks of *E. coli* O157:H7 in Canada (Ali,
20 2004). Similar phenomena might have played an important role in the emergence of Ebola,
21 HIV/AIDS and Marburg viruses (Daszak *et al.*, 2000). Moreover economic expansion is often
22 accompanied by a series of socio-economic changes, including population ageing, which can
23 also play an important role in increasing population susceptibility . Finally environmental change

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

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

7 **5 Causality from below: individual behaviour and infectious diseases**

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

Comment [g13]: Switch to disease ecology?

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

3

4 *5.1 Adaptive human behaviour*

5 McCallum *et al.* (2001) identify three factors which determine the rate at which new infections
6 occur in a given population: the contact rate, the proportion of contacts with susceptible
7 individuals and the probability that once an ‘appropriate’ contact has occurred, the infection will
8 be transmitted. If the contact rate between individuals is (at least partially) determined by
9 probability judgments and behavioural choices, then cross fertilization between economics and
10 psychology can provide useful insights. The recognition that an individual’s behaviour should be
11 explicitly included in models of epidemics is not new. A more interesting observation is that, at
12 least for directly transmitted diseases, human behaviour is likely to be adaptive as it will at the
13 same time affect and respond to the course of epidemics. Unfortunately to this date empirical
14 research, which explicitly matches adaptive behaviour to epidemics, is sparse (Fergusson, 2007).
15 In the case of HIV/AIDS, where the trade-off between engaging in desirable activities (e.g.,
16 frequently changing sexual partners) and the associated risk of contracting the disease is
17 particularly stark, evidence indicates how behavioural changes have occurred with the
18 progression of the disease prevalence (Becker and Joseph, 1988). Similarly, during the 2003
19 SARS epidemics in Hong-Kong individuals showed increased attitude to reducing social
20 contacts as the epidemics progressed (Lau *et al.*, 2005).
21 Although human behaviour is so important in the spread of a disease, and individuals alter their
22 behaviour when the disease progresses (as in this case also the probability of getting infected will
23 change), it is common to model behaviour as independent from prevalence, with empirical

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

Comment [g14]: Disease ecological-economic models?

17 5.2 Beyond *Homo Oeconomicus*

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

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

5 Infectious disease control has public good properties since, for whatever level of disease control
6 attained, everyone benefits regardless of whether they help meet the costs involved. These costs
7 are not only financial. For example, a vaccination program for swine flu might involve each
8 participant suffering a mild version of the symptoms of the pathogen, but the public health
9 benefits of this action (a small increment in 'herd immunity') accrue to the entire population.

10 Although there are private benefits from vaccination (self-protection), a person for whom self
11 protection is outweighed by the induced symptoms would not be expected to be swayed by the
12 public health rationale for vaccination. Moreover, an individual who has been infected may have
13 no rational choice reason at all to avoid infecting others, since he or she would incur the costs of
14 self-isolation, would not benefit from disease control, and might not feel sufficiently altruistic
15 towards the generality of the rest of the population to pay those costs.

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

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

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

3 Another important insight from psychology relates to the interactions between extrinsic and
4 intrinsic motivations and its implications for appropriate policy design. People are motivated to
5 do the right thing not only because of extrinsic motivations, but also for intrinsic rewards.

6 Extrinsic motivations refer to the set of incentives applied from outside and include both
7 economic incentives (e.g., changes in relative prices through taxes/subsidies) and regulatory
8 ones. Intrinsic motivations come from within the person (Deci, 1971). Although economists do
9 not deny the existence of intrinsic motivations, they normally assume that they can just be added
10 to extrinsic ones. Hence, introducing economic incentives will always generate the desired
11 behavioural changes. In the context of the consumer choice theory, for example, it is assumed
12 that changes in income and/or relative prices (i.e., the extrinsic motivations) will not affect the
13 shape of the preference maps (i.e., the intrinsic motivations which are taken as given). Empirical
14 results show how this is not always the case (Frey and Oberholzer-Gee, 1997; Bowles 2008).

15 This apparent paradox is explained through the motivational crowding-out effect. The
16 introduction of extrinsic motivations may in some cases lead to the weakening of intrinsic
17 motivations to such an extent that the total effect is a behavioural change in an undesirable
18 direction. For instance, in comparing voluntary and paid blood donation, supplies were more
19 forthcoming under the former regime, and the blood was also of higher quality (Titmuss, 1970).

20 Thus economic incentives triggered a crowding-out effect which, repressing the expression of
21 altruism on behalf of donors, created counterproductive effects in the “blood market”.

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

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

5

6 **6 Directions for future research**

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

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

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

17

18 $I_{t+1} - I_t = \eta(\cdot)(1 - I_t)I_t - \omega(\cdot)I_t \quad (1)$

19

20 Expression (1) is a good starting point for our discussion since it closely resembles a
21 conventional disease ecology model. This simple model states that the rate of change in infection
22 prevalence depends on the transmission rate (η) 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.

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

$$9 \quad I_{t+1} = f_1(I_t, E_t, C_t, T_t, Y_t, R_t) \quad (2.a)$$

10

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

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

18

$$19 \quad R_{t+1} = f_2(R_t, E_t, I_t, X_t) \quad (2.b)$$

$$20 \quad Y_{t+1} = f_3(Y_t, I_t, R_t, E_t, T_t, X_t) \quad (2.c)$$

$$21 \quad T_{t+1} = f_4(T_t, Y_t, R_t, X_t) \quad (2.d)$$

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

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

13

$$14 \quad E_{t+1} = f_5(E_t, Y_t, X_t) \quad (3)$$

15

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

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

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

10

11 *6.1 Characterizing adaptive human behaviour*

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

1 As the pay-offs are likely to be different for infected/infectious and susceptible individuals (and
2 as the proportions of each in the population change with changes in prevalence), the behavioural
3 variables will change with infection prevalence. The very fact that human behaviour is adaptive
4 indicates that it is dynamic and responsive to changes in the infection prevalence. The main
5 challenge in the future will be to collect data on person-to-person and person-to-animal contact
6 rates over a relevant period of time following an outbreak and try to understand how the contact
7 pattern responds to the infection progression. This could be done using ethnographic approaches
8 and/or diaries and surveys (Beutels *et al.*, 2006). Where the evolution of contact rates in a given
9 population at the time when an epidemic develops cannot be readily observed, suitable proxies
10 should be identified. For human infectious diseases for example, such proxies could include data
11 on public transport traffic (e.g., Bharti *et al.*, 2008), international travel data (Johansson *et al.*,
12 2011) and/or hours spent watching TV or engaging in other home activities (as opposed to
13 engaging in social activities). These considerations extend to the other relevant behavioural
14 variables (e.g., decision to take medical treatment or vaccination etc.).

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

20

21 *6.2 Characterizing the interactions between intrinsic and extrinsic motivations*

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

1 disease ecology models should account for both. This may seem an almost impossible task, as
 2 unlike extrinsic motivations (e.g., regulations and/or price mechanisms like fines and/or
 3 taxes/subsidies) intrinsic motives are difficult to quantify. However, as pointed out by Frey
 4 (1997), this is not necessarily a problem as long as one is able to characterize the relationship
 5 between intrinsic and extrinsic motives. Both sets of motives (we label intrinsic motives W and
 6 consider health policy R as an example of extrinsic motives) will have an impact on the
 7 behavioural variables. Again, for simplicity consider the social contact rate (C_t) as an example of
 8 behavioural variable. The role of extrinsic and intrinsic motives in shaping this variable can be
 9 captured as $\Delta C_t = C_{t+1} - C_t = f(\dots, W_t, R_t, \dots)$. Recent developments in behavioural economics (see
 10 Bowles 2008 for further references), show that extrinsic motivations may affect intrinsic ones so
 11 that $W_t = h(R_t)$. Consider for example the case in which a local government, in response to an
 12 epidemic of swine flu, is planning to introduce some regulations to restrict people's abilities to
 13 use public transport and/or to attend crowded places (e.g., bars, clubs etc.). If the introduction of
 14 such an extrinsic motivation interacts with the individuals' intrinsic motivations the total effect
 15 on individuals' behaviour can be written as

16

$$17 \quad \frac{d\Delta C}{dR} = \frac{\partial f}{\partial h} \frac{\partial h}{\partial R} + \frac{\partial f}{\partial R} \leq 0 \quad (4)$$

18

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

1 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
2 have the desired result of restricting personal contacts (this is the normal assumption in
3 mainstream economics)

4 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
5 regulation will be even more effective as extrinsic motivations ‘crowd in’ intrinsic ones.

6 c. $\frac{\partial h}{\partial R} < 0$: in this case the total effect will be weaker as extrinsic motivations ‘crowd out’
7 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
8 opposite direction than the intended one.

9

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

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

20

1 $C_{t+1} = f_5(C_t, I_t, Y_t, R_t, X_t)$ (5)

2

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

8

9 *6.3 Joint estimation of epidemiological and socio-economic responses*

10 This last point is a methodological one and relates to the specification of statistical/econometric
11 models required to correctly estimate the relevant parameters in the epidemiological-economic
12 model. It should be clear by now that the ecological and the socio-economic system form an
13 adaptive complex system organized in hierarchical levels, where processes occur at different
14 spatio-temporal scales. Such processes are interdependent and change over time, but possess one
15 over-arching feature which makes them attractive. This feature is that the lower-level entities are
16 each related, but only through the hierarchical nodes stemming from the spatio-temporal chain.
17 The interactions between the processes at a lower level are in this sense an emergent property at
18 the next level of organization. Perhaps the best way to capture these interactions is to use a
19 hierarchical econometric model (Wilke, 2003). The use of hierarchical models per-se in disease
20 ecology is not new (Duncan *et al.*, 1996; Diez Roux, 2000, 2008). As noted by Diez Roux (2000)
21 hierarchical models may be used to explain phenomena at the focal level by accounting also for
22 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.

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

12 At this stage the reader may feel frustrated, under the impression that our discussion simply
13 posits that everything is related to everything. On the other hand, the traditional analysis of
14 epidemiological phenomena ascribes the causality of emergence and spread clearly to one single
15 level³. In general the existing literature is cavalier about the possibility of feedbacks among the
16 various processes both within and between levels (Diez Roux, 2000 and 2008). Our approach, on
17 the other hand, follows from the recognition that in complex systems causality can be found
18 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.

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

16
17

18 **7 Conclusions**

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

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

21

22

23

1 **References**

2 Ali, S.H., 2004. A socio-ecological autopsy of the *E. coli* O157:H7 outbreak in
3 Walkerton, Ontario, Canada. *Social Science and Medicine* 58, 2601-2612.

4 Allen, T.F. & Starr, T.B. 1988. *Hierarchy: Perspectives for Ecological Complexity*.
5 University of Chicago Press.

6

7 Baltagi, B.H., Egger, P. & Pfaffermayr, M., 2003. A generalized design for bilateral trade
8 flow models. *Economic Letters* 80, 391-397.

9 Barber, L.M., Schleier, J.J. & Peterson, R.D.K., 2010. Economic cost analysis of West
10 Nile Virus outbreak, Sacramento County, California, USA, 2005. *Emerging Infectious Diseases*
11 16(3), 480-486.

12 Becker, M.H. & Joseph, G.J., 1988. AIDS and behavioural change to reduce risk: a
13 review. *American Journal of Public Health* 78, 394-410.

14 Beutels, P., Shkedy, Z., Aerts, M. & Van Damme, P., 2006. Social mixing patterns for
15 transmission models of close contact infections: exploring self-evaluation and diary based data
16 collection through a web-based interface. *Epidemiology and Infection* 134, 1158-1166.

17 Bharti, N., Xia, Y., Bjornstad, O.N. and Grenfell, B.T., 2008. Measles on the edge:
18 coastal heterogeneities and infection dynamics. *PLOS One*, 3(4).

19 Borghesi, S. & Vercelli, A., 2004. Globalization, inequality and health. *International*
20 *Journal of Global Environmental Issues* 4, 89-108.

21 Bowles, S., 2008. Policies designed for self-interested citizens may undermine “the moral
22 sentiments”: evidence from economic experiments. *Science* 320, 1605-1609.

1 Camerer, C.F. & Loewenstein, G., 2004. Behavioral economics: past, present and future.
2 In Camerer, C.F., Loewenstein, G., Rabin, M. (Eds), *Advances in Behavioral Economics*,
3 Princeton University Press, New York, p. 3-51.

4 Ceddia, M.G., 2012. Optimal disease eradication n sympatric metapopulations.
5 *Environmental and Resource Economics* 52(4), 499-530.

6 Chou, J., Kuo, N. & Peng, S., 2004. The potential impacts of the SARS outbreak on the
7 Taiwanese economy. *Asian Economic Papers* 3, 84-99

8 Chua, K.B., Lam, S.K., Koh, C.L., Hooi, P.S., Wee, K.F., Kong, J.H., Chua, B.H., Chan,
9 Y.P., Lim, Y.E., 2000. Reservoir of Nipah virus identified. *Proceedings of the International*
10 *Conference on Emerging Infectious Diseases*, Atlanta, USA, Session 78.

11 Cialdini, R., 1993. *Influence: science and practice*. HarperCollins, New York.

12

13 Daly, H., 1991. *Steady-State Economics*. Island Press, Washington D.C.

14 D'Onofrio, A., Manfredi, P., 2009. Information-related changes in contact patterns may
15 trigger oscillation in the endemic prevalence of infectious diseases. *Journal of Theoretical*
16 *Biology* 256, 473-478.

17 Daszak, P., Cunningham, A., Hyatt, A.D., 2000. Emerging infectious diseases of wildlife
18 – threats to biodiversity and human health. *Science* 287, 443-449.

19 Daszak, P., Cunningham, A.A., Hyatt, A.D., 2001. Anthropogenic environmental change
20 and the emergence of infectious disease in wildlife. *Acta Tropica* 78, 103-116.

21 Deci, E.L., 1971. Effects of externally mediated rewards on intrinsic motivation. *Journal*
22 *of Personality and Social Psychology* 18, 105-115.

23

1 Diez Roux, A.V., 2000. Multilevel analysis in public health research. *Annual Review of*
2 *Public Health* 21: 171-192.

3 Diez Roux, A.V. (2007). Integrating social and biological factors in health research: a
4 systems view. *Annals of Epidemiology* 17: 569-574.

5 Diez Roux, A.V., 2008. Next steps in understanding the multilevel determinants of
6 health. *Journal of Epidemiology & Community Health* 62: 957-959.

7 Drezè, J.H., Richard, J.F., 1983. Bayesian analysis of simultaneous equation systems. In
8 Griliches, Z., Intriligator, D. (Eds.), *Handbook of Econometrics, Volume 1*, North-Holland, p.
9 517-598.

10 Dry, S., 2008. Epidemics for all? Governing health in a global age. *STEPS Working*
11 *Paper 9*, Brighton: STEPS. Available at <http://www.steps-centre.org/PDFs/Epidemics.pdf> (last
12 accessed on 22/10/2011).

13 Duncan, C., Jones, K., Moon, G., 1996. Health-related behaviour in context: a multilevel
14 modelling approach. *Social Science and Medicine* 42: 817-830.

15 Fenichel, E.P., Castillo-Chavez, C., Ceddia, M.G., Chowell, G., Gonzalez Parra, P.A.,
16 Hickling, G.J. *et al.*, 2011. Adaptive human behaviour in epidemiological models. *Proceedings*
17 *of the National Academy of Science* 108, 6306-6311.

18 Fergusson, N., 2007. Capturing human behaviour: understanding the dynamics of
19 infectious disease transmission demands a holistic approach, yet today's models largely ignore
20 how epidemics change individual behaviour. *Nature* 446, 733.

21 Frederick, S., Loewenstein, G., O'Donogue, T., 2004. Time discounting and time
22 preference: a critical review. In: *Advances in Behavioral Economics* (ed. Camerer, C.F.,
23 Loewenstein, G. & Rabin, M.). Princeton University Press, New York, p. 162-222.

1 Frey, B.S., 1997. *Not just for the money. An economic theory of personal motivation.*
2 Edward Elgar Publishing, Cheltenham, UK.

3 Frey, B.S., Oberholzer-Gee, F., 1997. The cost of price incentives: an empirical analysis
4 of motivation crowding-out. *The American Economic Review* 87, 746-755.

5 Haacker, M. (Ed.), 2004. *The macroeconomics of HIV/AIDS.* Available at
6 <http://www.imf.org/external/pubs/ft/aids/eng/> (last consulted on 20/10/2011).

7 Jones, K.E., Patel, N.G., Levy, M. A., Storeygard, A., Balk, D., Gittleman, J.L. *et al.*,
8 2008. Global trends in emerging infectious diseases. *Nature* 451, 990-994.

9 Johansson, M.A., Arana-Vizcarrondo, N., Biggerstaff, B.J., Staples, J.E., Gallagher, N.,
10 Marano, N., 2011. On the treatment of airline travelers in mathematical models. *PLOS One*, 6(7).

11 Lau, J.T.F., Yang, X., Pang, E., Tsuy, H.Y., Wong, E., Wing, Y.K., 2005. SARS-related
12 perceptions in Hong Kong. *Emerging Infectious Diseases* 11, 417-424.

13 McCallum, H.I., Barlow, N., Hone, J., 2001. How should pathogens transmission be
14 modelled? *Trends in Ecology and Evolution* 16, 295-300.

15 Mossong, J., *et al.*, 2008. Social contacts and mixing patterns relevant to the spread of
16 infectious diseases. *PLOS Medicine* 5(3).

17 Patz, J.A., Epstein, P.R., Burke, T.A., Balbus, J.M., 1996. Global climate change and
18 emerging infectious diseases. *Journal of the American Medical Association* 275, 217-223.

19 Pearce, N., Merletti, F., 2006. Complexity, simplicity, and epidemiology. *International*
20 *Journal of Epidemiology* 35, 515-519.

21 Peiris, J.S., Yuen, K.Y., Osterhaus, A.D., Stöhr, K., 2003. The severe acute respiratory
22 syndrome. *The New England Journal of Medicine* 349, 2431-2441.

1 Perrings, C., Fenichel, E., Kinzig, A., 2010. Globalization and invasive alien species:
2 trade, pests and pathogens. In Perrings, C., Mooney, H., Williamson, M. (Eds.), *Bioinvasions*
3 *and Globalization. Ecology, Economics, Management and Policy*, Oxford University Press, p. 42-
4 55.

5 Pimentel, D., 2005. Environmental and economic costs of the application of pesticides
6 primarily in the United States. *Environment, Development and Sustainability* 7, 229-252.

7 Pimentel, D., Zuniga, R., Morrison, D., 2005. Update on the environmental and
8 economic costs associated with alien-invasive species in the United States. *Ecological*
9 *Economics* 52, 273-288.

10 Popper, K., 1990. *A World of Propensities*. Thoemmes Press, Bristol, England.

11 Price-Smith, A.T., 2002. *The Health of Nations: Infectious Disease, Environmental*
12 *Change and Their Effects on National Security and Development*. MIT Press.

13 Prigogine, I., 1978. *From being to becoming*. W.H. Freeman and Co., San Francisco.

14 Reluga, T.C., 2010. Game theory of social distancing in response to an epidemic. *PLoS*
15 *Comput Biol* 6, e1000793.

16 Rosen, R., 1977. *Life itself: a comprehensive inquiry into the nature, origin and*
17 *fabrication of life*. Columbia University Press, New York.

18 Rubin, G.J., Amlot, R., Page, L., Wessley S., 2009. Public perceptions, anxiety and
19 behavior change in relation to the swine flu outbreak: cross sectional telephone survey. *British*
20 *Medical Journal* 339, b265.

21 Titmuss, R.M., 1970. *The gift relationship*. London: Allen and Unwin.

22 Ulanowicz, R.E., 1997. *Ecology, the Ascendent Perspective*. Columbia University Press.

1 Ulanowicz, R.E., 2009. *A third window – Natural life beyond Newton and Darwin*.
2 Templeton Foundation Press.

3 Whyte, L.L., Wilson, A.G., Wilson, D. (Eds.), 1969. *Hierarchical Structures*. American
4 Elsevier Publishing Company, New York.

5 Wilke, C.K., 2003. Hierarchical Bayesian models for predicting the spread of ecological
6 processes. *Ecology* 84, 1382-1394.

7 Wilkinson, K., Grant, W.P., Green, L.E., Hunter S., Jeger M.J., Lowe P. *et al.*, 2011.
8 Infectious diseases of animal and plants: an interdisciplinary approach. *Philosophical*
9 *Transactions of the Royal Society B* 366, 1933-1942.

10 Wilson, M.E., 2001. Environmental change and infectious diseases. *Ecosystem Health* 6,
11 7-12.

12 Woolhouse, M., 2011. How to make predictions about future infectious disease risks.
13 *Philosophical Transactions of the Royal Society B* 366, 2045-2054.

14 Zaghegni, E., Billari, F.C., Manfredi, P., Melegaro, A., Mossong, J., Edmunds J.W.,
15 2008. Using time-use data to parameterize models for the spread of close-contact infectious
16 diseases. *American Journal of Epidemiology* 168, 1082-1090.